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ANGLO-AMERICAN SYMPOSIUM ON PSYCHOSURGERY, NEUROPHYSIOLOGY and PHYSICAL TREATMENTS IN PSYCHIATRY

ORGANISED BY

THE COUNCIL OF THE SECTION OF PSYCHIATRY

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FOREWORD

As since the war no opportunity had presented itself for British and American colleagues to meet and discuss the problems arising from the recent developments in Psychosurgery, Neurophysiology and Physical Treatments in Psychiatry, the Officers of the Section of Psychiatry of the Royal Society of Medicine profited by the occasion of the Fourth International Neurological Congress to invite eminent American workers to visit England on their way home from Paris and to deliver papers before the Section.

The invitations were accepted and fully attended series of meetings were held to which leading British workers in these fields were invited to take part in the discussions.

These meetings did much to develop appreciation of each other's work by confrères of both nationalities and they proved to be of such interest as to make publication *in extenso* desirable.

The Council of the Royal Society of Medicine thereupon decided to publish this Supplement to the *Proceedings* of the Society. In this matter the Council gratefully acknowledges the very practical help of Dr C. Charles Burlingame of the Institute of Living, Hartford, Connecticut, who, by arranging the purchase of a sufficient number of copies for distribution in the United States of America, made publication by the Royal Society of Medicine not only possible but also successful.

The Officers of the Section of Psychiatry wish to record their deep appreciation of the many others whose preparatory work contributed to the success of the Symposium, and of the Editors and Staff concerned with the publication of this fasciculus.

J. R. Rees,
President, Section of Psychiatry of the Royal Society of Medicine, 1948–49.

Denis Hill,
William Sargant,
Honorary Secretaries, Section of Psychiatry of the Royal Society of Medicine, 1948–49.

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[*September 12, 1949*]

FIRST SESSION

CHAIRMAN

J. R. REES, C.B.E., M.A., M.D., F.R.C.P., D.P.H.

RECENT TECHNIQUES IN PSYCHOSURGERY

TOPECTOMY

By Professor J. LAWRENCE POOL

Professor of Neurological Surgery, Neurological Institute, New York

It gives me great pleasure indeed to offer this brief Address on the subject of topectomy. I should like to say at the outset that I make no claim to being a psychiatrist, although I became interested in the subject of psychosurgery, and particularly in the work of Dr Walter Freeman, with a view to a more specific approach in frontal lobe operations than was possible by lobotomy. My colleagues and I have accordingly made efforts in this direction about which I would like to speak.

'Topectomy' is perhaps a poor term. We coined it in the interests of conciseness, to get away from 'subtotal bilateral prefrontal lobectomy'. Dr W. Penfield of Montreal has used 'bilateral frontal gyrectomy', which is an equally good or better term.

The topectomy operation consists of bilateral frontal cortical ablation or gyrectomy. We started with the idea of ablating part of Brodmann's area No. 9, as it had been observed by Mettler that behaviour changes in animals were most predominantly associated with bilateral ablation of that area of the cortex rather than with ablation of areas Nos. 10, 11 or 12.

Following our initial pilot cases in 1946–7, a more formal study of the procedure was carried out at the large State hospital in Greystone Park, N.J. Here under a team of investigators directed by Dr Fred Mettler we proceeded to study the effects following ablation of different cortical areas according to Brodmann's chart. We chose that chart for convenience, without supposing it to be a correct chart or one which represents definite physiological functions. In the course of the study, in which areas forward of the motor cortex were removed as symmetrically as possible, Dr R. G. Heath, my psychiatric colleague, and I thought that the best results with the minimal intellectual and emotional deficit were obtained following removal of cortex from Brodmann's areas Nos. 9 and 10. We then proceeded with the cases reported here, confining our removals to the region of the cortex which we believed to be Brodmann's areas Nos. 9 and 10.

This is a brief report on the first 52 patients who have had from one year's to three years' follow-up. They are patients chosen from almost all psychiatric ranges and categories, and about 50% of them were from the so-called 'back' wards of the State hospitals. Most of them were schizophrenics.

The procedure is carried out in one stage under sodium pentothal anesthesia. A coronal scalp incision and single bone flap are made which provide an excellent view of much of each frontal lobe. The cortical tissue is excised down to the bulk of the white matter, but no incision into the white matter is made. The cortex is removed as a block, which provides a means of estimating its extent and volume. We have weighed every specimen. We have also measured each cavity, which gives a fair idea of the volume as an added check. We think that the quantity of tissue removed is extremely important and that quantity is important in different categories of psychiatric illness. For instance, with the chronic schizophrenic, if improvement is to take place at all, a

larger amount of tissue must be removed than in the depressive case or in the case in which the patient is not afflicted with mental illness at all but undergoes an operation for the relief of pain. In the severe psychotic states we feel that 30 to 35 grammes must be removed from each side. Usually, if they do not improve, and additional cortex is removed or subsequently isolated, these patients seldom show any further improvement. We have removed 30 to 35 grammes from each side in the case of the chronic schizophrenic, 20 to 25 grammes in the compulsive or depressive states, and approximately 15 to 20 grammes in the pain cases. Thus there seems to be a definite quantitative factor. Indeed, a too extensive removal in the non-psychotic patient may produce profound personality changes, which is also the experience of many operators doing leucotomy.

As to the appearance of the cortex: the topectomy operation because of its generous exposure provides an opportunity for a fairly good look at the lateral or convex surface of each frontal lobe. To most of us it seems that gross abnormalities are present in at least 50% of the schizophrenic group in particular. We do not think that this is necessarily correlated with age or even shock therapy, because some of the gross changes have occurred in a few patients in whom no shock therapy had been carried out. The changes are characterized by a gross appearance of cortical atrophy with widened sulci and very narrow gyri, while the arachnoid is thickened. The cortex may be yellowish in appearance and extremely hard on cross-section with the scalpel blade.

Microscopic studies have, however, shown no significant abnormal changes so that the apparent gross changes are so far unexplained.

Electro-encephalography has been done on all patients before operation, and was normal in all, but after the operation there are almost invariably abnormal changes in the prefrontal and precentral areas for a period of four to six weeks. After that such changes generally disappear, but in a few cases, as in those who have developed seizures, the changes have persisted.

In cases where a further operation has been carried out, records have been made from the margin of the previous incision, and such records, according to Dr Paul Hoefer, have shown no abnormal patterns. No patients with seizures, however, have been investigated in this way. The incidence of post-operative seizures following this operation has been higher to date than the incidence following lobotomy. In some series after lobotomy the incidence of seizures has been approximately 10%, and in others 12%. In this series of 52 cases 14% have had two or more seizures, but they have been controlled by appropriate medication.

There have been no operative fatalities in the 52 cases of this series nor in the total of 125 topectomies now done. The mortality rate therefore, so far, is zero. Two patients have had post-operative extradural hemorrhages, treated promptly by evacuation so that both have made an excellent recovery.

A number of lantern slides illustrating the operation were then shown, the speaker saying: The incision is carried down medially along the falx near the superior margin of the cingulate gyrus. The procedure is most easily accomplished by clipping the appropriate branches of the anterior cerebral artery. A clean incision with the knife blade at right angles to the surface is then made. With a sharp spatula the block is lifted out cleanly. A small-bore sucker tube is used to smooth the edges of the cavity, hemostasis is secured, and the wound closed.

In 15 cases before the cortex had been excised the anterior portion of the cingulate gyrus was electrically stimulated because of current interest in this region, and because of its supposed autonomic representation demonstrated by the work of Wilbur K. Smith and others in animals. In all our cases we have obtained almost exactly the same type of results as Smith in the laboratory animal.

In one case, when separating adhesions between the cingulate gyri, a marked irregularity in the respiratory rate occurred. Other changes were characterized by alterations in the pulse rate and the blood pressure which may rise or fall temporarily. In two cases temporary apnea appeared of extremely brief duration and in a third case an accelerated respiratory rate occurred up to 60 a minute, with a gradual return to 20 in the course of an hour. Such changes may occur singly or in combination with other autonomic effects, such as dilatation of the pupils. I mention this because this is the first time these effects have been demonstrated in man.

In our opinion and in the opinion of some who have seen our cases, the adverse effects of topectomy are probably less than in successful cases of lobotomy. I was very much struck by that fact in several patients seen after an interval of one or two years after topectomy. They maintained their normal family and business life even though they showed slight changes such as a tendency to distractability. The one complaint of an ex-patient whom I met in Paris the other day was that sometimes he could not remember a name.

In conclusion, topectomy is a procedure which has been devised in the interest of developing a more specific operation than the old-fashioned type of lobotomy. I have described the technique and mentioned some of the side-effects. While we have a higher incidence of epilepsy, the operative mortality rate has been zero.

SELECTIVE CORTICAL UNDERCUTTING

By W. B. Scoville, M.D.

Neurosurgeon Hartford Hospital and the Institute of Living. Assistant Clinical Professor of Surgery, Yale University. Hartford, Connecticut

I wish to say how honored I am in being invited to share in this Discussion. Since the introduction of the standard lobotomy by Moniz in Lisbon and Freeman in America, there has been a general acceptance of some form of lobotomy and its variations as a form of therapy in the more severe psychoses. Concomitantly, those doing large numbers of lobotomies have found an appreciable blunting of the personality resulting from the standard operation especially in the realms of imagination, foresight, ambition and social sensitivity. This has been stressed by Rylander. The blunting is not noticeable in those severe, deteriorated schizophrenics of long standing but if we are to apply this operation to the affective psychoses, psychoneuroses and intractable pain cases, it is imperative that psychosurgery result in no appreciable blunting. Lobotomists already appreciate this and various methods of more selective limited lobotomies are in the process of development.

Pool (who has just spoken) together with the Greystone Group has done pioneer work in the United States with his cortical ablations or topectomies. In England, neuro-anatomists, physiologists and surgeons have done yeoman service largely in selective leucotomies consisting of selective sectioning of various quadrants of white matter connecting the frontal lobes with the thalamus. Smith, Dax and Reitman believe that the cutting of the inferior quadrants (orbital connexions) affects the personality differently from cutting of the superior quadrants (connexions from areas 9 and 10 of Brodmann). They believe that orbital leucotomies have made their patients 'light and gay' while the superior leucotomies have had somewhat the opposite result. This has *not* been confirmed by the speaker. Freeman, after first introducing the standard lobotomy to the United States, has recently introduced the transorbital lobotomy, sometimes vulgarly known as the 'ice pick operation', and is of the opinion that there is distinctly less personality change along with an appreciable benefit in early cases of schizophrenia, affective psychoses and tension states.

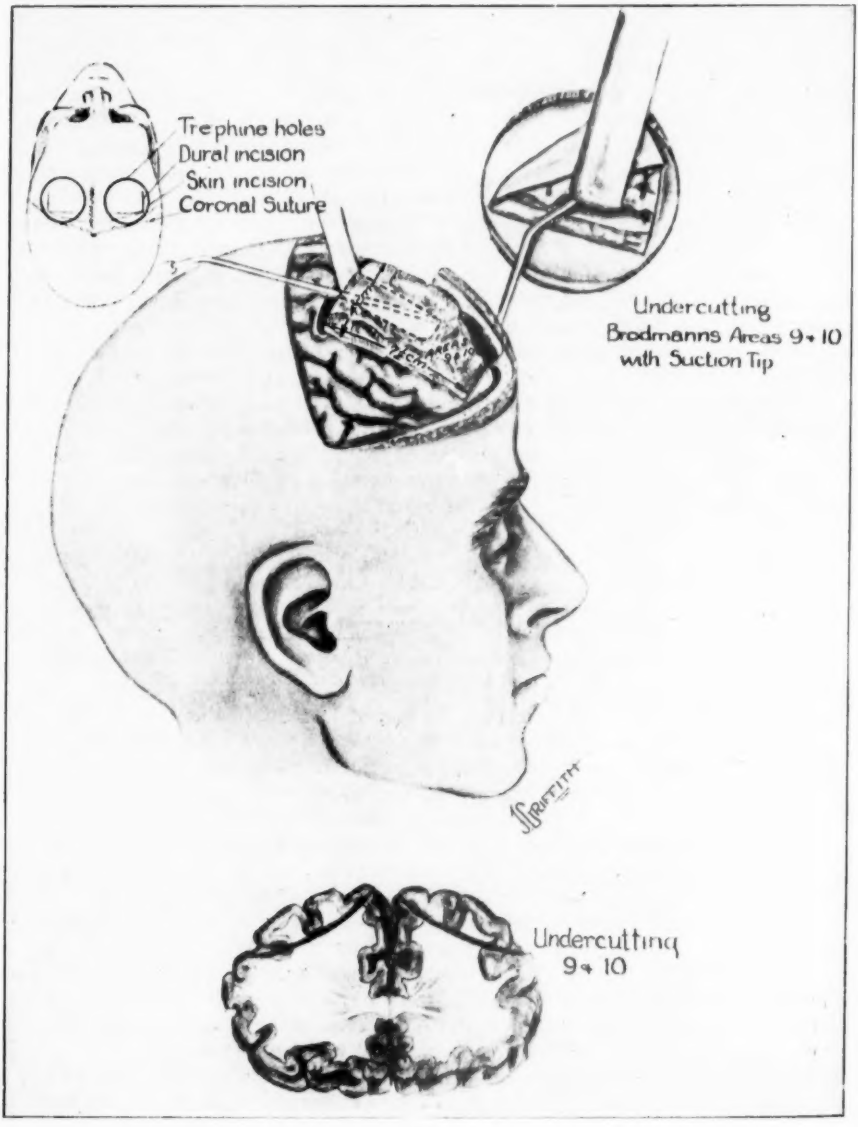


FIG. 1.—Cortical undercutting of superior convexity (Brodmann's areas 9 and 10).

Wycis and Spiegel in the United States as well as Puech and David in Paris have developed a most ingenious method of great research interest in their direct selective destruction of thalamic nuclei by a Horsley-Clarke stereotaxic instrument.

Let us compare the frontal lobes and their thalamic connexions to a telephone switchboard with its connecting cable to various telephones. Pool with his topectomy actually cuts out sections of the switchboard proper. Smith, Dax and Reitman with their superior and orbital leucotomies have cut parts of the telephone cable. Wycis

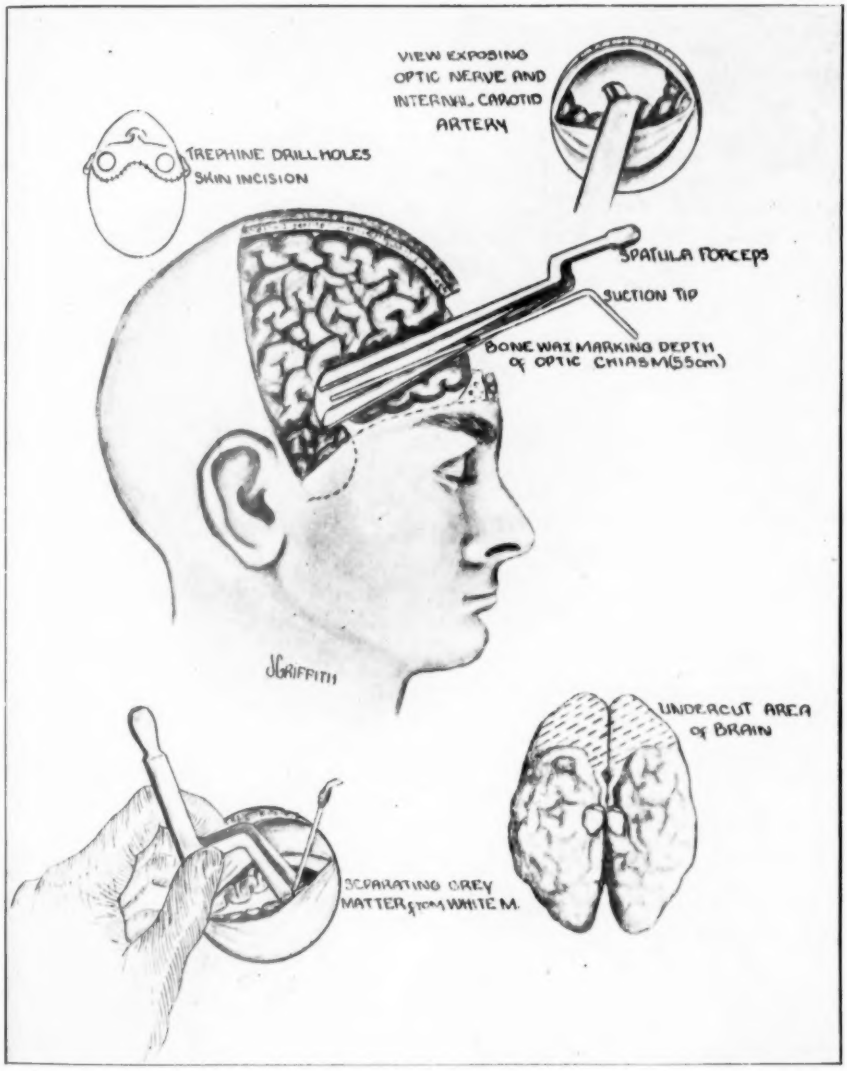


FIG. 2.—Orbital undercutting.

and Spiegel with their thalamotomy have cut out a considerable number of the telephones and the speaker with his selective undercutting has stepped behind the switchboard and cut the wires connecting various portions of it to the cable. Selective cortical undercutting therefore constitutes a method of functional and anatomic isolation of various areas of the frontal cortex without interference of its own or adjacent blood supply. The technique consists of making a line of cleavage by a brain spatula and fine suction tube at the relatively avascular junction of grey and white matter with interruption of both long and short association fibers to the thalamus and to the adjacent frontal cortex. This operation was first described at the

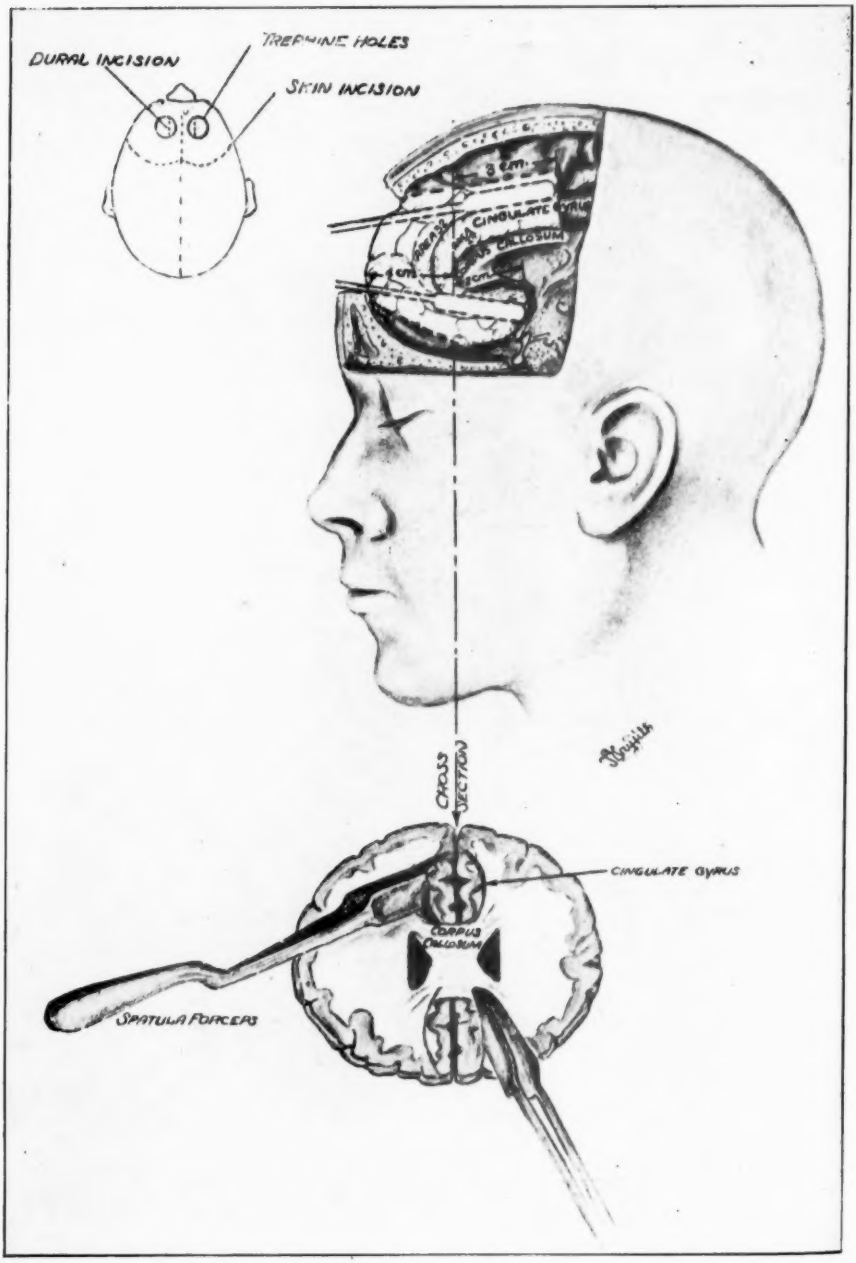


FIG. 3.—Cortical undercutting of medial surface (cingulate gyrus).

International Congress of Psychosurgery in Lisbon in August 1948 and again in the January 1949 issue of the *Journal of Neurosurgery*, **6**, 65.

We have arbitrarily selected three equal surface areas for undercutting, each area measuring some 50 sq. cm. as opposed to 160 sq. cm. of surface area which is isolated by a standard lobotomy. One operation consists of undercutting of the superior convexity (partial Brodmann's areas 9 and 10). Another undercuts the entire orbital surface including the prechiasmal area. Another undercuts the medial surface including the entire rostral cingulate gyrus both above and below the corpus callosum. The first area was selected because of the benefit following ablation of this same area by Pool in his topectomy. The second and third areas were selected because of the animal experiments of McCulloch, Walker, Fulton, Bailey and the neuro-anatomic studies of Le Gros Clark and Meyer. Le Gros Clark, in *Lancet*, 1948 (i), 353, in three scant pages presented succinctly more factual observations on the connexions of the frontal lobes than his American colleagues seem to have been able to do in some fifty articles (a very slight exaggeration in order to promote Anglo-American relations!). Profound personality and autonomic changes have resulted from ablations and stimulation of both the posterior orbital and the anterior cingulate areas in animals including sham rage (Fulton) in cats and loss of social conscience (Ward) in monkeys.

Technique

(Slides were Shown Illustrating the Surgical Technique and Locations of the Incisions for Each of the Three Operations, *see* figs. 1, 2 and 3, on pp. 4, 5 and 6.)

There are certain technical advantages in this operation over cortical ablations, especially in the preservation of adjacent blood supply. 95% of the blood supply of the cortex occurs from the surface inwards. Other advantages are the absence of raw exposed surfaces and greater speed and facility of operation inasmuch as the procedure does not require exposure of the total area to be undercut and can be done through $1\frac{1}{2}''$ or $2''$ trephine buttons.

Results

We have performed the operation of selective cortical undercutting on 124 patients[1] in two Connecticut state hospitals (Middletown and Norwich), the Institute of Living and the Hartford Hospital for 5 cases of intractable pain, 17 affective psychoses, 6 psychoneuroses and 96 schizophrenias. Follow-up studies have been from one to twenty months. Isolated early seizures, promptly aborted by medication, have occurred in 10% of the cases. There have been two deaths, four post-operative hemorrhages and no infections. In the schizophrenic patients, significant improvement occurred in an equal number subjected to (1) undercutting of the superior convexity (48%); (2) undercutting of the orbital surface (52%); and (3) standard lobotomies (47% of 40 control patients). Undercutting of the medial surface and cingulate gyrus resulted in a fewer number (25%) with significant improvement. In summary, for the schizophrenic cases the results of undercutting of both superior convexity and orbital surface have been equal and roughly comparable to a standard lobotomy but with appreciably less blunting of the personality. Undercutting of the cingulate gyrus has given less satisfactory results and has proved technically more difficult.

In the affective psychoses, especially the agitated depressions and the obsessive-compulsive psychoneuroses with tension, universal improvement has resulted from all forms of undercutting as well as from standard lobotomies in a control series. Cases with intractable pain have been benefited to the extent of marked relief from worry, anticipation of pain and addiction. A warning must be given that lobotomies and undercuttings performed on non-psychotic 'pain' patients exhibit far more obvious personality deterioration than any occurring in psychiatric patients. Hence, only a limited undercutting should be performed and standard bilateral lobotomies should not be used.

There have been remarkably few physiologic and personality changes following cortical undercutting even of the cingulate gyrus and prechiasmal area: no sham rage,

[1]As of December 1949.

hypermotility or prolonged stupor. Temporary vomiting and transitory drowsiness occur in cingulate undercutting. Breath holding follows manipulation but not undercutting of the cingulate area. Profound autonomic changes including postural edema, tachycardia, blood pressure lability and fever did occur in two 'cingulate' undercut patients who were found to have large subcortical blood clots adjacent to the corpus callosum. These abnormal signs cleared upon draining the clots through needle punctures. Such abnormalities did not occur to even a minor degree in 38 other 'cingulate' cases, suggesting that adjacent pressure or vascular damage was the cause of these phenomena.

Conclusions

A plea is made for more selective types of lobotomy. It is felt that ablations or precise undercutting of various areas of the frontal cortex under direct vision present the best chance for determination of the exact physiologic function of the various portions of the frontal cortex. To date, we have found little specificity of function in the three areas undercut suggesting to us that the changes following lobotomy, both total and selective, have been quantitative rather than qualitative.

It is felt that a sufficiently large series of cases has been studied to make tentative recommendations for the therapeutic application of selective undercutting: (1) Orbital undercutting is the ideal operation for severe psychoneurotic patients because of its technical facility and almost complete absence of personality blunting. (2) Undercutting of the superior convexity works well for certain types of pain and addiction. (3) Orbital and superior convexity undercutting each appears to benefit the affective psychoses and schizophrenic psychoses. (4) Cingulate gyrus undercutting will be used for research rather than therapeutic application. (5) Standard lobotomy will be reserved for the 'hopeless' deteriorated schizophrenic patients of years' duration.

TRANSORBITAL LEUCOTOMY: THE DEEP FRONTAL CUT

By Professor Walter Freeman, M.D., Ph.D.

From the Department of Neurology and Neurological Surgery
George Washington University, Washington, D.C.

Transorbital leucotomy was introduced by Fiamberti [1] a year after the original work of Egas Moniz [2], but attracted little attention until 1947, and even then there was no report of the validity of the method. It was satisfactorily demonstrated, however, that the method was quick and safe, and within the capacity of the psychiatrist who had familiarized himself with the landmarks. A year ago I [3] reported the use of this method in 100 cases without fatality. Since then the series has been increased to more than 350, with 2 fatal hemorrhages and 2 deaths from other causes. In the paper I stressed the fact that transorbital leucotomy was useful in the middle ground of patients, namely, in those that do not maintain their improvement after more conservative methods of treatment, and yet who are not considered sufficiently intractable to warrant the major operation. Furthermore, it was clearly evident that transorbital leucotomy could not influence favorably the large number of chronic schizophrenic patients who were naturally considered for operation. In view of the consistent record of failure in these cases, further studies were undertaken on the cadaver to ascertain whether the incisions could safely be extended so as to sever a larger proportion of the radiation from the thalamus to the frontal pole. It proved easier than could have been anticipated. Merely by elevating the handle of the instrument when the point was in a certain position within the frontal lobe, it was possible to sever this radiation opposite the head of the caudate nucleus, and without additional danger to important vessels.

TECHNIQUE

Very little preparation is necessary for transorbital leucotomy, only that which applies to the administration of electroshock. The patient is given from two to five successive electro-convulsive shocks in order to maintain a state of coma for about five minutes. When the last convulsion subsides, the nurse places a towel over the nose and mouth to prevent contamination by saliva or nasal secretions. The operator draws the upper eyelid away from the eyeball and inserts the point of the transorbital leucotome into the conjunctival sac, moving the point around until he finds the vault of the orbit. This is about 3 cm. from the mid-line. He then aims the shaft of the instrument parallel with the bony ridge of the nose and taps the base with a hammer to drive it through the orbital plate. Usually this is easily accomplished. At a depth of 5 cm. from the margin of the upper eyelid, the point of the instrument is 3 cm. within the frontal lobe. The operator pulls the handle as far laterally as the conformation of the orbit will permit. This severs fibers in the basal portion of the thalamofrontal radiation.

He returns the handle of the instrument to an oblique position, directed somewhat medially, in order to avoid arteries in the lateral aspect of the frontal lobe and frontal operculum, and continues tapping on the base of the instrument until the 7 cm. mark is reached. Here he again checks the position of the instrument, bringing it parallel with the bony ridge of the nose, and, if a record is desired, photographing it in situ (fig. 1). At this point, in order to sever the thalamofrontal radiation in the superior

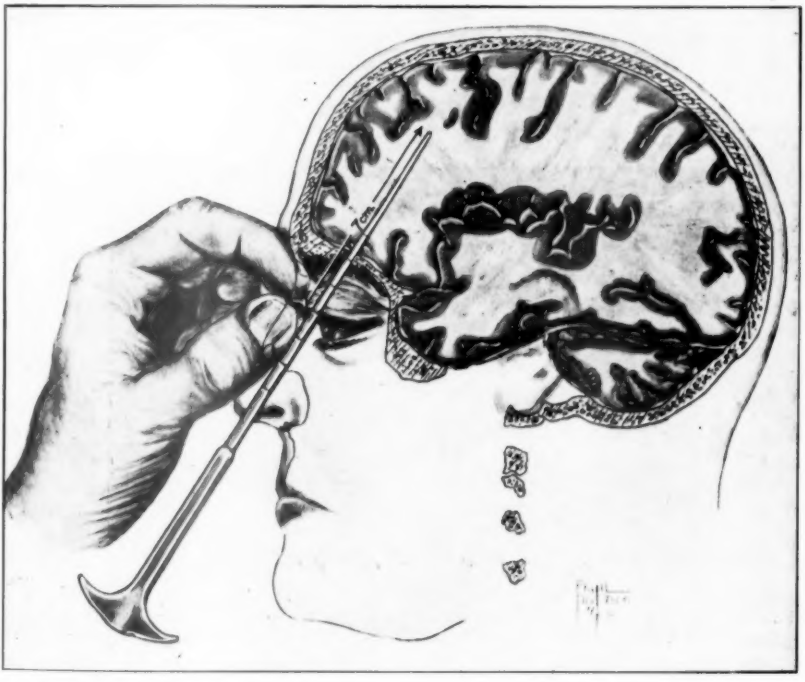
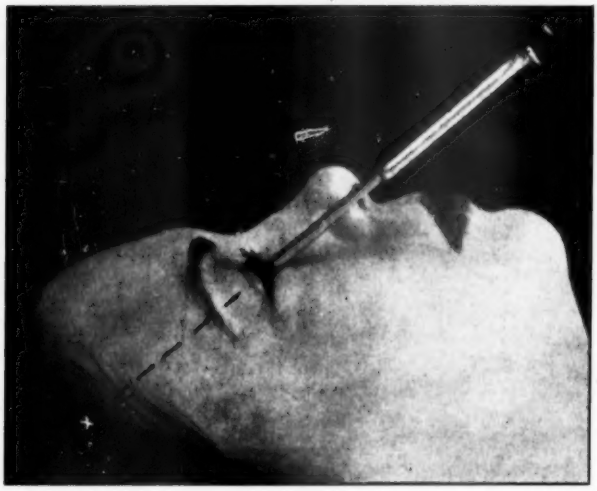


FIG. 1.—Drawing showing transorbital leucotome at the 7 cm. mark in the plane of the bony ridge of the nose.

portion, underlying areas 9 and 10 of Brodmann, he moves the handle 20 degrees medially and 30 degrees laterally from the parasagittal plane. Standing behind the head of the patient, he then strongly elevates the handle of the instrument in this

oblique plane until the shaft lies as nearly as possible parallel with the orbital plate. Finally he returns the handle to the parasagittal plane and checks again, to determine either visually or photographically how closely he has approached his aim (fig. 2A



A

B

FIG. 2.—Photograph of patient with leucotome in (A) the initial cut, (B) the deep frontal cut.

and B). He then withdraws the instrument, applying pressure upon the upper eyelid to control escape of blood and cerebrospinal fluid into the orbital tissues.

Results

The deep frontal cut, in successful cases, severs the thalamofrontal radiation opposite the head of the caudate nucleus (fig. 3). Not infrequently the incisions penetrate the

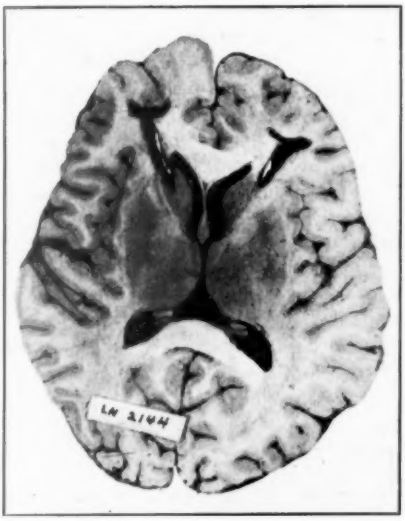


Fig. 3.—Horizontal section of brain showing incisions made in white matter by transorbital leucotomy. The deep frontal cut interrupts most of the fibers from the thalamus to the frontal poles.

ventricle, but this appears to be harmless. Fig. 3 shows both the superior incisions and the deep frontal cuts. This specimen was obtained from a patient who died of carcinoma shortly after operation. The operative field lies almost entirely in the subcortical white matter and is practically bloodless. The deep frontal cut varies greatly from case to case, depending upon the thickness of the orbital plate. In some instances, when the transorbital leucotome is thrust through the orbital plate with a mere tap of the knuckle, there is no difficulty at all; in other cases, however, the plate is so thick and heavy that the operator risks bending or breaking the instrument. Quite often there is a sudden 'give' or even an audible crack as the orbital plate fractures. It is remarkable how little reaction there is to such an occurrence. Usually there is no greater degree of swelling or ecchymosis than after the simple operation. Sometimes a small quantity of blood and cerebrospinal fluid escapes, like bloody tears, for an hour or two. Only once has there been cerebrospinal rhinorrhea lasting for ten days, and only twice have infectious complications occurred, both in connexion with post-operative intracerebral hematomas, from which both recovered. Penicillin in oil and wax is used in prophylactic fashion in all cases.

The effect of the deep frontal cut upon the patient undergoing transorbital leucotomy is somewhat more marked than that which follows the simpler operation first described, but less than that which follows major leucotomy. However, within a day or two orientation is regained and the patient is usually discharged to his home on the day following operation. Relaxation and inertia are evident from the time the patient wakes up. Vomiting occurs in half the cases, incontinence seldom, and masked face and plateau speech are indicative of complications.

Transorbital leucotomy has a range of effectiveness that is quite comparable with that of major leucotomy. It is useful in cases of chronic schizophrenia, involutional

psychoses, obsessive tension states and severe chronic pain of terminal carcinoma. While it fails in deteriorated patients, it is almost on a par with the major operation. Of fifteen patients having first the transorbital operation then followed by major leucotomy, only three derived further benefit. Insufficient time has elapsed for assessment of long-range results, but thus far they are satisfactory.

SUMMARY

By means of a new twist, termed the deep frontal cut, transorbital leucotomy can be made as extensive anatomically and as effective clinically as major frontal leucotomy.

The method has the advantages of simplicity, speed and safety, and can safely be entrusted to the psychiatrist who will familiarize himself with the landmarks.

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This paper was accompanied by a film, a copy of which is obtainable from the Honorary Secretary of the Section of Psychiatry, Royal Society of Medicine, Dr William Sargant, at 1, Wimpole Street, London, W.1.

THALAMOTOMY – NEUROSURGICAL ASPECTS[1]

By Dr. H. T. WYCIS and Professor E. A. SPIEGEL

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For nearly half a century the stereotaxic apparatus of Horsley and Clarke has been used in experimental animals in order to produce subcortical lesions without significant injury to the overlying structures. Curiously enough this method has not been applied to the human skull and brain prior to our first communication [1]. The chief reason for this seems to be the following: In the animals usually used for this method (rat, cat, and monkey) it is sufficient to rely on the relationship between the co-ordinates of the skull and the part of the brain to be injured because of the constancy in the shape of the skull. In the human the great variability in the shape of the skull precludes such a simple method of application. In the method developed by us (stereo-encephalotomy) we have attempted to overcome the variability of the skull by using a landmark within the patient's brain as a reference point, namely, visualization of the pineal gland by roentgenography. If this structure is not calcified then structures such as the suprapineal recess, etc., in the neighborhood of the pineal gland are delineated by pneumo-encephalography.

The apparatus which we have called the stereo-encephalotome consists of two parts: a superstructure and the base. The base consists of a ring upon which is mounted a plaster cast of the skull prepared for each individual patient. The superstructure is a four-legged frame with a needle carrier which allows the electrode to be moved in any plane. A newer modification eliminates the plaster cast and anchors the base of the stereo-encephalotome to the skull by means of four rubber plugs or by four stainless steel pins which are inserted into small drill holes of the skull. The base of the apparatus is aligned so that its frame is parallel to a line drawn between the inferior border of the orbit and the external auditory canal. As already mentioned, the co-ordinates of the apparatus are referred to a point within the brain, namely, the

[1] This paper was accompanied by a film.

pineal gland. The patient is x-rayed with the apparatus in position and the relationship of the pineal gland to the electrode is established.

In order to be able to reapply the base at operation in exactly the same position as it was during roentgenography, the following precautions are taken. An additional superstructure containing five movable pins (one at the intersection of the sagittal and interaural planes; two in the sagittal plane; and two in the interaural plane) is mounted to the base, and the points of the scalp touched by the pins are tattooed before roentgenography. Furthermore, the distance between the upper end of the tubes, in which the pins are movable, and the corresponding tattoo marks is measured. Before the operation the base has to be reapplied in such a way that the pins exactly touch the tattoo marks and that the above-mentioned distances are the same as at the time of roentgenography.

If the pineal gland is not visualized then a pneumo-encephalogram is done and the electrode is oriented with reference to the suprapineal recess or other structures in the neighborhood of the third ventricle. With this data and the aid of brain specimens sectioned in the planes of the stereo-encephalotome one can compute the co-ordinates necessary to produce the lesions desired, for instance, the dorsomedial nucleus of the thalamus (thalamotomy) or the spinothalamic tract in the mid-brain (mesencephalotomy).

Under local or endotracheal nitrous oxide-ether anesthesia with the patient in a semi-sitting position, the apparatus is applied. An 8 cm. transverse scalp incision is usually made in the interaural plane. A trephine opening is made just to the right or left of the mid-line and the superior longitudinal sinus is exposed. The superstructure is applied to the base and the mid-line identified. The dura is punctured 6–7 mm. lateral from the mid-line, and the electrode is lowered at this point according to the measurements obtained from the roentgen film. Lesions may be made either by electrolysis using direct current or by electrocoagulation by using a high-frequency current of the Davis-Bovie unit. Two types of electrodes may be employed. Where a small spherical lesion is desired the electrode consists of a hollow stainless steel tube through which passes an insulated wire bared at its tip for a distance of 1·5 mm. Where several large lesions are desired the electrode consists of an outer insulated tube through which passes a stainless steel stylet. The stylet pierces a small lateral opening in the outer sheath and protrudes at an angle for a distance of 3 mm. The stylet may be withdrawn and the entire electrode rotated. In this manner one can make several rosettes of lesions at any desired level all through a single puncture. With this electrode the lesions are produced by electrolysis. When the final lesion is made a droplet of pantopaque or lipiodol may be instilled through the stainless steel tube and its position verified by x-ray post-operatively. In some instances where there is residual air in the ventricle one can ascertain the position of the electrode by recording subcortical potentials as the electrode passes through the lateral ventricle.

The results will be discussed by Professor Spiegel (page 84, Session IV).

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Discussion

Mr Wylie McKissock (London) said that his own experience had been confined to the 'blind' method of prefrontal leucotomy carried out on the Freeman and Watts original technique. He had now personal experience of over 1,400 cases and his assistants had experience of over 500 so that between them they had had a little less than 2,000 cases, and during a period of nine years had seen little reason to alter the technique from a purely therapeutic angle.

In the last year a different method had been adopted which in many ways was extremely similar to that of Scoville's but it was only applicable, in his opinion, to patients suffering from chronic obsessional states or from severe agitation and depression.

The point which had struck him particularly was the fact that although they had heard a series of entirely different methods of carrying out these procedures, the results showed a very remarkable similarity, and that similarity was carried over to the 1,400 cases in his own series. Roughly speaking, there was the same incidence of remission of schizophrenia, recovery in the agitated depressive and melancholic cases, and chronic depressive states. These different approaches to the same problem were of extreme value from the research point of view.

He had certain criticisms to make. Firstly, dealing with Professor Pool's paper, it seemed that in excising this area of cortex in the way he did, he was not producing a pure excision of the area which was removed. In other words, in order to remove that area he had to divide the blood supply to the adjacent brain. When he had the privilege of seeing Professor Pool perform this operation last year Professor Pool was quite confident that the blood supply to the middle frontal convolution was being impaired if not completely cut off. In addition, this operation was one of considerable magnitude – probably a minor point. Scoville's method was one which he and his colleagues had been practising, or at least a very similar form, for the past nine months and it avoided the particular defect of Pool's operation in that by undercutting, certainly in the way it was done now, it was possible to save the arteries from the mid-line, literally sucking out the white matter and leaving the vessels intact so that one was producing a much more pure abolition of the functions of areas 9 and 10 by undercutting and leaving the main vessels intact. He inclined very much to Scoville's method although he would confine its use to patients suffering from chronic obsessional neuroses or extreme agitation. His own experience had not led him to believe that it would be a useful operation in schizophrenia.

He was fascinated by the extraordinary ingenuity attained by Professor Spiegel and Dr Wycis in their operation and hoped they would give some idea of the nature of the results produced by this method. He would be inclined to assume that they would be similar to the other methods of leucotomy. Undercutting only was the most promising line to follow at the present time although for all therapeutic purposes he still thought that the 'blind' operation which they had been practising for nine years and which had produced good results was the simplest of them all. He did not think it required any more complicated set-up or technique than the very dramatic transorbital method which Professor Freeman had shown that afternoon. He must admit that his neurosurgical principles were gravely upset by the method described and even more by the fact that it should be done by a psychiatrist. Nevertheless, the results had shown that this method, properly used, could produce good results. It was, he thought, a potential defect that the instrument used was blunt and the frontal lobe was a great deal more mobile than people were inclined to realize. If a blunt instrument was introduced into the frontal lobe and moved, the frontal lobe would move a considerable distance in any direction in which the instrument was used so that although the steel pin might be introduced into the lobe it did not necessarily mean that a large amount of white matter was being divided. He thought the pictures showed a very much smaller lesion than he would have anticipated from the degree of movement through which the instrument was moved from one side to the other and therefore a very much smaller leucotomy was being produced than one might think. This also applied, he believed, to the 'blind' method of leucotomy in which sometimes singularly little effect was produced although the needle had moved through the usual range and he thought this was due to the fact that the frontal lobe had moved with the instrument.

He was particularly attracted by Scoville's method. He had done something very

similar through a pair of burr holes on either side of the mid-line just in front of the coronal suture – he incised the superior frontal convolution transversely and then sucked out a thin layer of the white matter down to the orbital plate. It could be made as wide as one wished, normally he made it 2–2·5 cm. wide and 6–8 cm. deep so that it was an extremely limited type of section. As it was done under direct vision any interference with the function of the brain on either side was prevented.

In the small series of cases carried out the results had been infinitely better than by any 'blind' leucotomy, very much less side-effects had been produced (personality change, that is) and he intended to direct attention more to undercutting than to the other methods which had been discussed.

When sufficient time had elapsed and the long-term results of these different methods had been collated and published they would be in a very much stronger position to decide what was the best surgical method to adopt in this newly developing branch of surgery and psychotherapy.

In conclusion he would like to say how much he had appreciated the attendance of these speakers from America.

Mr E. J. RADLEY-SMITH (London) said: As a matter of historical interest, at the end of 1942 he and his colleagues began to investigate the value of selective cuts and actually on February 19, 1943, they performed the first selective leucotomy. That was a horizontal incision above the cortex of the orbital plate, something very much more crude but not dissimilar to the method described by Dr Scoville because they were aiming at the same position. Since that date he had found more and more psychiatrists were working for selective cuts instead of a very wide complete cut and today he carried out a very considerable number of selective cuts, both the low vertical cut and others.

However accurate one was with all these 'blind' methods it was impossible to say precisely what one was cutting. He agreed with Dr Wycis who said that he preferred a surface marking on the brain rather than on the bone. However carefully one marked the bone none of these methods could be entirely satisfactory because of the disparity between bony and cerebral topography. Taking a point on the brain could make the matter slightly more accurate, or by filling the ventricles with air, but there was such variation in the size of the anterior horn of the lateral ventricle that they were still inaccurate in their cutting by any method.

This led him to say that the operation of excision of cortical areas as described that afternoon had much to recommend it from the point of view of accuracy. He had a very slight experience of topectomy, he had carried out six such operations in eighteen months, and although it was a very much bigger neurosurgical proceeding Professor Pool reported no mortality and he himself had not had any to date. Professor Pool was very distressed with the high incidence of epilepsy after this procedure and no doubt he too would come across that complication when he had done more cases.

He had performed a few of Freeman's transorbital leucotomy operations and he would agree with Mr McKissock that he had the feeling extremely strongly that the frontal lobe was moving on the instrument and that he had not been cutting as much as he thought he was cutting.

Mr HARVEY JACKSON (London) said that the various methods would appear to be somewhat of the same nature throughout, that is, some interference in the thalamo-frontal connexion of the brain. Each and all of these methods were applied for the same purpose but in their application surgical principles were changing to some extent. One of the main surgical principles to be considered when dealing with patients was to do as little as possible but as much as was necessary. With this in mind one wondered where was the advantage to be gained from these different surgical procedures. What in fact did one wish to do ?

In the anterior part of the brain all the fibres were approximated before their distribution to the frontal cortex, near to the thalamus. One could, therefore, attempt to interfere with the tract near to the thalamus or near to the cortex, but the same object underlay all the procedures. The method of partial section in a more anterior part of the brain than the thalamus, and a less peripheral part of the brain than the cortex, could offer a great deal, and one knew from the work of Radley-Smith that it was possible to get as much as one wanted on selective section as by a total resection. One had to realize that even with leucotomy there was not controlled destruction of tissue. If, as Mr Radley-Smith now advocated, an encephalographic examination was carried out before and after operation, one found varying amounts of damage to the brain. After all, one wished to do as little damage as possible. One could by going to the cortex limit it within certain margins, but damaged blood supplies meant further destruction.

In his own experience, which did not include these other methods, he had found some evidence of the relief which leucotomy could offer in the majority of cases. One of his greatest difficulties working with psychiatrists in this country was their reference to different states when really they were tackling one and the same thing: a state of tension arising out of mental disorder. If that could be relieved, the patient was able to rationalize his symptoms in better ways, so much so that finally his tension-state would fade into the background and no longer have the same importance. Consequently, the patient was more able to deal with his imbalance. How remarkable it was to see the patients after leucotomy, in whom the blood pressure was reduced, the pulse rate altered, the breathing altered, and there were other disturbances, e.g. incontinence. (This is probably not the ordinary form of incontinence, it did not come on immediately after the operation but about thirty-six hours afterwards, and he believed that this was evidence of autonomic damage.)

If the same results could be achieved with a partial section there was a good deal to be said for a restricted leucotomy. Leucotomy had been carried out largely with straight instruments and if that was done the incision must be fan-shaped, hence a full division of the white matter could not be made. These remarks also applied to transorbital leucotomy. Whatever one might feel about the surgical procedure, if one was approaching through the orbital plate, putting in a straight instrument, the major division would lie superiorly. One was led to believe that it was the tissue overlying the orbit which had to be divided to give adequate results. How would Dr Freeman explain the satisfactory results which he obtained when there was such a restriction of the amount of white matter divided over the orbital region.

In respect of the question of previous treatment, he still felt that what Dr Scoville described as the changes one saw in the brain, a very much shrunken brain, a large collection of fluid, the yellowish colour of the cortex and its firmness were indications of an altered brain. When one had come across these brains one wondered what the pathology behind it was; as far as psychiatry was concerned there was no pathology, but when one saw a brain $\frac{3}{4}$ in. away from the dura it could not be said to be normal. Although a certain amount of cortical atrophic change in schizophrenic conditions might be expected he was somewhat anxious that this should not be added to by psychiatric treatment. One feared lest these repeated courses of convulsive treatments were creating a condition which would lead to a state almost comparable with repeated cerebral contusion, the patients were confused and did not know what was going on. The very fact that often the electro-encephalogram did not show changes was not of any definite significance. Usually it was not until there were major distortions of the ventricular system that the electro-encephalogram would reveal disordered activity. He had often wondered whether the EEG really gave a fair idea of the underlying condition.

Dr Scoville had given figures relating to the manifestations after operation which

caused him some apprehension. In his own experience of leucotomy cases which he had followed up a figure of 4% incidence of post-operative epileptiform seizures applied. He had had an extraordinary case of a man who was extremely destructive, he was submitted to leucotomy, he did not respond satisfactorily and as it was an early case in his series he performed a secondary leucotomy and the patient did extremely well. Some time after operation he resorted to his destructive methods again and one felt rather disappointed that he was returning to his previous psychotic state until it was suggested that this may be evidence of an epileptic equivalent. He was treated with anti-convulsive medication and had not been affected by further destructive episodes.

The emotional picture was reflected in the physical picture. He had a patient with diabetes, his blood sugar was not controlled in any way, yet following leucotomy absolute control of his diabetes could be maintained. One had to consider these physical changes because one had to consider how far one could go and the route of selection.

Dr Freeman had said that 50% of his cases were non-institutional, we did not get that in this country, we deal with institutional cases. We were not dealing only with relief of the patients but an economic situation whereby there was not the staff to look after them, and if these dirty, destructive individuals could be turned into more amenable creatures who could look after themselves we felt we were doing something worth while although the patients did not return to their ordinary social status.

The therapeutic side of the problem was important, but this work must go on if they were to search for better and more satisfactory results. He felt from the mass point of view that there was a great deal to be said for using restricted leucotomy.

Mr JAMES HARDMAN (Sheffield) entirely agreed with what Mr Harvey Jackson had said about the benefits of the use of the standard prefrontal leucotomy operation. Fractional frontal section had a very important place in the treatment of these cases, results were obtained without getting deteriorated patients. Very occasionally one had a deteriorated patient, but the aged, agitated melancholic could be cured by a lower quadrant leucotomy, without any deterioration, the patients returned to their homes and their families were delighted.

He had a feeling that excision of areas 9 and 10 was not likely to give a satisfactory result, because it was well known that destruction of this region of the brain in monkeys and various animals caused marked restlessness and distractability, and he had seen the same phenomena, though fleeting, in patients after excision of areas 9 and 10. In his limited experience of 7 cases, the hallucinations had not altered in any appreciable way and the patients had not improved. He was, therefore, at a loss to account for the good results reported by Professor Pool and his associates. Only one of his patients who had an excision of areas 9 and 10 had improved, this patient had recurrent mania, and in this instance the operation encroached upon area 32, which might be the reason for this patient's improvement.

He had carried out topectomy of area 13, or the inferior surface of the frontal lobe, on 3 katatonic schizophrenic patients. In a previous paper given before the Royal Medico-Psychological Association at York, July 21, 1949, he had reported that the results in these cases were not very good, but since then one of these patients had been discharged from the mental institution and in the family home she appeared to be readjusting herself very well, though it was now only three months since operation. The operation which he felt may be the operation for the future, was the bilateral excision of the gyrus cinguli and lips of the adjoining sulcus, that is, a partial removal of area 24 and area 32. He had carried it out on 12 cases and on every occasion the patient had shown a remarkable improvement. When making this assertion it should be stressed that the last case had been operated on only three months ago. The majority

of these cases were early ones, not degenerated schizophrenics, they were intelligent and some had not been institutionalized; such patients could do very well. Mr Harvey Jackson had stressed that leucotomy was an operation designed to take out the emotional tension of the psychotic illness; excision of the gyrus cinguli might remove this tension without alteration in the personality.

Finally, he wondered how all these various surgical manoeuvres worked, nothing had been heard yet about the function of the brain. Surely this should be considered, it was the thing in which they were all interested, it was their common ground, and he was hoping that a great deal would be heard about functional brain circuits when Professor McCulloch gave his paper. He would not go further in this direction, but would put in a plea for the emotional circuit described by Papez ten years ago. This involved the temporal lobe, the hippocampus, the fornix, the mammillary bodies, the bundle of Vicq d'Azyr, the anterior nucleus of the thalamus, which then projected through the anterior part of the internal capsule round the ventricle on to the gyrus cinguli. It had been shown that area 24 projected with the rest of the brain's suppressor strips on to the lips of the sulcus cinguli. One could not help wondering what this system of suppression had to do with emotional states, and the working of the cerebrum as a whole. The answer to all this may have an important bearing on the understanding of the pathological physiology of the psychotic states, but this was for the future.

Mr GEOFFREY KNIGHT (London) said that his experience so far had been confined to the various methods of prefrontal leucotomy. It was obvious that a price had to be paid for the benefits to be derived from major leucotomy, a price that was measured in terms of diminished mental capacity, and diminished capacity for enjoyment; this price was well worth while if the psychotic symptoms were severe, but was definitely not worth while in a less severe state of psychotic illness. He had tried to modify the amount of blunting and diminution in the capacity for enjoyment by employing anterior cuts and also by confining his section to the lower fibres of the lobes. He believed that by using such methods it was possible to obtain considerable improvement in selected cases with far less blunting and with far fewer undesirable effects. However, any form of leucotomy did introduce some of these features and therefore these more selective methods had a great deal to recommend them.

As to the relief of pain by these selective methods, undercutting seemed to be the most rational procedure for general use because it did not interfere with the blood supply of the brain, as Mr McKissock had pointed out. It did not need any elaborate apparatus, but did it produce as great an effect on the relief of pain as the standard or modified leucotomy? Recently in his neurosurgical unit they had been trying minor leucotomy for the relief of rather an interesting group of cases: those patients who suffered from persistent chronic headache without organic cause which formed part of a syndrome of depression in which headache was the principal and leading symptom. In the cases which had been dealt with by minor leucotomy the results had been strikingly good and that might be a minor field in which these restricted operations could be used. Would undercutting have as good an effect on pain as leucotomy?

Dr R. E. HEMPHILL (Bristol) stated that the contributions to the Symposium could be considered from two angles – therapy and psychiatric research. It emerged from everything that had been reported that leucotomy had some value in almost every psychiatric condition in which it had been performed. In schizophrenia this was 40 to 50% relief, irrespective of the length of history or the form of schizophrenia. As the various modifications of leucotomy or lobotomy had not markedly altered

the average percentage of relief in schizophrenia, there could not be much discussion about the relative value of procedures in this condition, from the point of view of therapy.

It was therefore clear that the selection of cases was most important, for if relief in schizophrenia was only 40 to 50%, what happened to the other 50 to 60%? One must postulate wide variations either in the clinical condition or in the surgical operation. All the neurosurgeons stressed that the operation produced physiological results and significantly altered emotional states. As these were the therapeutic aims, he suggested it should be possible to devise physiological tests to indicate how the vegetative system had been affected by the operation.

Where a similar operative technique was employed, other factors, such as mental constitution and disposition, would have to be looked for to explain discrepancies in results. The fact that psychological tests had failed to show precisely the effects of leucotomy, even in the fields of intelligence and application, indicated how difficult it was to draw scientific conclusions from therapeutic results alone.

It was suggested that as a research measure carefully selected patients should be subjected to topectomy, for in this operation there was precise anatomical control. The results could then be assessed in comparable clinical material. It did not serve a useful purpose to include cases of obsessional neurosis and depression with schizophrenia.

Professor Pool had described how brain size seemed to vary in schizophrenia, suggesting that there was something special about its pathology. Perhaps the therapeutic results could be correlated with the degree of shrinkage remarked on. As there was believed to be nothing specific about brain histology in schizophrenia, one must enquire how the apparent shrinkage would be accounted for. If it was atrophy, it did not involve to any extent structures which could be seen, and one must assume it to be due to changes of the background substance related to the chemical content of brain.

Perhaps research could be undertaken from the point of view of the steroid chemistry of brain in schizophrenia, making use of topectomy, and the results correlated with macroscopic and histological findings. He would like to ask Professor Pool if the statement made by Kirschbaum, and earlier by Elvidge and Reed, on histological changes in brain biopsy material in schizophrenia, had been confirmed by him.

Dr TURNER MCLARDY (London) said that he and his colleagues in the Department of Neuropathology, Institute of Psychiatry, had investigated some 120 leucotomized brains from all over the United Kingdom and he would underline all that had been said with regard to the high probability of movement of the brain with the leucotome in many cases. He had no doubt whatsoever that that was one reason for the tremendous unintentional variability of the cut so often revealed by post-mortem dissection. A striking illustration was to be found in the two cases described in the *Lancet* (1949) (ii), 465. Here the standard transorbital manipulations had resulted in no lesion beyond the track made by the initial insertion of the instrument. As to its explanation, in talking to neurosurgeons he had been impressed by their unanimity regarding the variability of the resistance to cutting between one brain and another, and he would throw out the suggestion that investigation should be made, e.g. by air-encephalography into the possible influences of anaesthetics and other transient circumstances on the volume and consistency of the brain before and after one frontal lobe had been traumatized, in psychotics of different types and in non-psychotics. The experimental method of White and his associates (*Arch. Surg.*, 1942, **44**, 1) might be pursued with profit.

This brought him to the extremely interesting remark of Dr Pool on apparent atrophy of the frontal lobes. He himself had examined five brains in which gross atrophic

appearances had been described at operation, but in which nothing abnormal whatsoever had been found post mortem macroscopically or microscopically. This evidence of transient shrinkage would again suggest some 'functional' lability in the consistency of the brain especially in the schizophrenias. It might offer a valuable starting-point towards elucidation of physico-chemical abnormalities in the brains of 'functional' psychotics.

Finally, he would utter a warning regarding the 'deep cut' modification of the transorbital operation. Among the 120 'standard' leucotomy cases already mentioned, after elimination of hæmorrhagic deaths, there was a highly significant correlation between death within five months of the operation and the finding of bilateral appreciable damage to extra-prefrontal structures, particularly the striatum, the premotor area and possibly area 13 of the posterior orbital region. The specimen passed round the meeting by Professor Freeman to demonstrate the 'deep cut' showed very appreciable damage to the head of the caudate nucleus on one side. Presumably such damage may as easily occur bilaterally and so determine 'delayed operative death' within a few months.

Dr CUNNINGHAM DAX (Surrey) said that mention had been made of selective leucotomy. He had treated 7 cases with bilateral incisions 1 cm. in diameter and up to date 3 of them had been discharged and 3 would probably be able to leave later on.

With regard to pain, he had had a clergyman with a three years' history of trigeminal neuralgia and drug addiction following an ophthalmic herpes; an incision 2·4 cm. in diameter was made above the orbital cortex and he hoped to return the patient to his parish duties fairly soon.

He would like to ask Dr Scoville which particular incisions he made in his cases with pain.

Professor POOL, in reply to the discussion, said that he only partly agreed with Mr McKissock. He thought Dr Scoville's procedure was the simplest but he proposed to continue his own procedure not because he thought it excelled, but because it provided an opportunity for certain studies in which he was interested and also for electrical stimulation when the opportunity offered. As to Mr McKissock's remarks with regard to circulation, the speaker did not think that widespread circulatory changes necessarily followed cortical ablation, because studies of the cortex both macroscopically and microscopically at the margins of the previous cortical ablation showed no changes beyond 1·5 cm. around the zone of excision.

With regard to Mr Hardman's question on the cingulate gyrus in the Columbia-Greystone series, the cingulate gyri were subtotally removed bilaterally, sparing the anterior cerebral arteries. The patient definitely showed profound autonomic changes for two and a half weeks with a complete return to the initial state of cold, clammy extremities and a poor peripheral circulation. Post-operatively there were also marked gastro-intestinal troubles manifested by vomiting, and even faecal vomiting. She became no better at any time after the operation. This raised the question as to whether or not in the good results reported after cingulate gyrus ablation, it was the type of case which was important. Perhaps in some cases that region of the cortex might be removed without improvement, while in others it might lead to improvement.

As to the question of destructibility of the personality following ablation it was his own opinion that when the ablations were carried out too far posteriorly, severe changes were likely to ensue. Thus patients with successful results had maintained their jobs although other men had been fired; another patient, since topectomy, had written a well-received magazine article, and a U.S.A. Government employee had been promoted since his operation.

Dr Hemphill raised a question with regard to pathology as to whether the anesthesia might be the explanation. Professor Pool thought, however, that the changes seemed too extensive to be accounted for by this factor.

Dr SCOVILLE, in reply to Mr Wylie McKissock, stated he was in 100% agreement with all of his remarks especially in his belief that all selective operations were largely quantitative rather than qualitative. The standard operation is probably still necessary in the malignant schizophrenics but should not be used in involutional melancholics or psychoneurotic patients. Precise selective operations will be of vast importance from a research point of view. In the initial schizophrenic breaks occurring in young people as well as in affective psychoses, any type of selective lobotomy will result in marked improvement; hence, he objected to the inexactness of the transorbital lobotomy and the radical extensiveness of the standard lobotomy when applied to these more benign psychoses.

The series of Smith, Dax and Reitman have been instructive in promoting interest in 'selective' leucotomies but here too he felt that the procedure lacked precision because of the concentration of fibres at the site of their sections. Only ablation or undercutting of precisely measured surface areas, under direct vision, can ever result in complete exactitude of selective interruption of frontal lobe connexions to the thalamus.

He was under the impression that all types of lobotomy will give roughly the same incidence of epilepsy with the possible exception of thalamotomy (low) and topectomy (high) if isolated early seizures are included in the statistics and listed by competent observers.

Selective lobotomies for pain are probably quantitative rather than qualitative and work by removing anxiety, addiction and anticipation and memory of pain rather than by the interruption of any specific pain centers in the frontal lobes or by change in skin thresholds for pain. This applies to both orbital and superior convexity undercutting.

In reply to Dr McLardy, Dr Scoville said that undercutting of area 13 and area 24 had not caused delayed death or deterioration.

In answer to Dr Cunningham Dax, he said that undercutting of superior convexity (5 cases) worked well; undercutting of orbital surface (1 case) not quite so well, but both had the same effect in lessening anxiety, and anticipation of pain without changing the skin threshold for pain.

Professor FREEMAN, in reply, said he thought that Mr Harvey Jackson had summed up the discussion as nicely as anybody when he said: Do as little as possible but as much as is necessary. With regard to some of the points which had been raised he thought the objection to the transorbital method was hardly a matter for professional wailing, the dangers were minimal. There were 2 cases where fits occurred, both these had hemorrhages. Of 15 patients having first the transorbital operation and then the major operation carried out, only 3 had benefited. For patients on the road to deterioration there was not much use in operating; one should operate when the patients were still fighting and there was a possibility of personality restoration. Watts and he were apart on the value of transorbital lobotomy in the relief of unbearable pain, because 5 out of 6 operated on by the transorbital method were failures, but later it was found that pain could be relieved by the deep frontal cut. He remembered one old man about 65 who had suffered pain from 1914 onwards after a blow. Transorbital lobotomy relieved his pain and he went back to work.

As far as lateral movement of the brain was concerned, this definitely happened especially where the brain was atrophied. It was not of particular significance in the deep frontal cut.

With regard to senile patients his oldest patient was 87.

Dr WYCIS, replying, said he thought it should be kept in mind that schizophrenia was not cured by any operation, it was a generalized disorder; it was not linked to any specific system with which one could interfere by these operations. All these operations seem to relieve tension, fear and anxiety, but – and this was a big 'but' – what else did they do? The frontal lobe operations distorted a patient's personality and that was what he and Dr Spiegel had tried to avoid with thalamotomy. They wished to alter the patient's tension and fear without seriously interfering with his personality structure.

With regard to post-operative convulsions, among all his cases there had been one instance of epileptic seizure which probably was not due to the operation. The psychologic and physiological results would be given in some detail in Dr Spiegel's communication. With the exception of a few instances of memory disturbances and impairment of initiative, thalamotomy did not result in a serious personality disturbance. It had been stated that it was important to have a fixed landmark in the brain and not on the skull and that was the principle of their method. They had often been asked how they knew where they were; one way was to check the position of an opaque dye injected into the lesion, by x-ray post-operatively; a second method was to record the electrical potentials of the subcortical structures as the needle entered the ventricle; if air was in the ventricle from a preceding encephalogram a high electrical resistance was encountered and 60-cycle activity was picked up. The final method was, of course, examination of post-operative deaths. Fortunately for the patients but unfortunately for him there were not enough deaths, but they were now studying a group of carcinoma cases and shortly they would have controls.

In reply to Mr Hardman's question, one has some knowledge of the functions of the hippocampal system in animals but it seems premature to apply these findings to man. As a matter of fact several years ago Dr Spiegel found in acute experiments that lesions of this system induced a condition of rage.

On the problem of pain he was interested in the problem of producing lesions in the dorsomedial nucleus of the thalamus, hoping to obtain results similar to those of Drs Freeman and Watts after prefrontal lobotomy. The patients did not complain about the pain only as long as they were in a state of confusion and disorientation. It was decided therefore only to make lesions in the spinothalamic tract in the midbrain. They were able to produce a contralateral analgesia without other disturbances by stereo-encephalotomy; thus showing that this method is sufficiently accurate. Dr Spiegel would give the results with regard to vegetative functions, *see* p. 86, Session IV.

[*September 12, 1949*]

SECOND SESSION

CHAIRMAN

W. REES THOMAS, M.D., F.R.C.P., D.P.M.

CLINICAL ASPECTS OF PSYCHOSURGERY

THEORETICAL ASPECTS OF FRONTAL LOBOTOMY AND SIMILAR BRAIN OPERATIONS

By PAUL H. HOCH, M.D.

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Many questions arise in connexion with observations made on lobotomized patients. The first question is whether or not frontal lobotomy and similar operations are specific or non-specific. We know organic and emotional influences are able to alter psychotic and neurotic disorders. Intercurrent diseases often have a beneficial influence on mental sickness. Therefore, it would not be too strange to assume that traumatization of the brain by operative procedure can have the same effect. If that were the case, any operation on the brain regardless of location would be able to produce similar results as reported by frontal lobotomy. We believe that this question can be answered in the negative.

Operations were performed on the skull and on the surface of the brain in a sufficient number of patients who in contrast to lobotomized patients did not show any improvement. We, therefore, concluded that frontal lobotomy and similar operations which interrupt cortical connexions have a certain specificity and cannot be replaced by *any* brain operation.

Those who thought that intellectual function and especially certain emotional behavior patterns are localized in certain parts of the frontal lobe began to operate from the point of view of localization of function.

Pool and Heath tried to correlate some of the brain function with the Brodmann areas. Operations were performed on different areas and claims were made that areas 9, 10 and 46 fulfil a specific function in the frontal lobe. We think that a sufficient number of patients showed improvement who were operated upon in other areas than those mentioned above to throw some doubt on this hypothesis.

Areas 9, 10 and 46 (topectomy) or areas 9 and 10 (transorbital) if operated upon achieve good results not because they are functionally the most important areas in the frontal lobe, but because of the large number of cortical thalamic fibers which pass through that region.

If we look over the claims and counter-claims which were made for different operations, the following thoughts emerge: (1) Are these observations qualitative in a sense that a certain area in the brain has a specific function? (2) Are the operations quantitative? Does this mean a certain amount of cortex has to be removed or its connexions severed to produce observable results? If this is true, then it would be irrelevant as to where the operation is performed. The results would be the same. Only a definite quantitative reduction of cortical function would be necessary. A

quantitative operation eliminates or diminishes the amount of cortical or thalamic areas functioning by cutting intercortical or corticothalamic connexions.

Today the connexions between the frontal lobe and the thalamus are especially emphasized. However, it is necessary to recall that the long association fibers connecting the cortical areas of different lobes are also of great importance. These connexions within the cortical areas and with the thalamus explain why, after frontal lobotomy, the alterations of psychic functioning are comparatively small. The basic intellectual and emotional functioning of the individual remains intact after frontal lobotomy, even though the more subtle cognitive and conative performances may be interfered with. If the basic functions of the person were to be concentrated in the frontal lobes, we could expect very serious alterations of the personality function after frontal lobotomy. This, however, is much less than prior theories on the function of the frontal lobe have indicated. Most likely when parts of the frontal lobe are separated from the other parts of the brain, the other cortical areas are able to take over. We conclude, based on observations on operated patients, that the basic intellectual and emotional life of the individual which is necessary for his personality functioning is not localized in the frontal lobe alone, but is distributed all over the cortical areas and in the corresponding thalamic regions. This does not exclude the possibility that the highest symbolic functions – creativeness, planning, and the fusion of emotional and intellectual performances are performed by the frontal lobe. Furthermore, the diffuse distribution of psychic functioning in the thalamus and brain cortex does not mean that the brain always acts as a whole, but that these functions are distributed and safeguarded by a diffusion of this function all over the cortex. There are concentrations of function in certain areas and these certain areas can interfere more than others in the psychic function of the individual. However, the hypothesis that elementary intellectual and emotional functioning can be localized in certain areas, and that centers exist for basic personality traits and drives is not tenable. The circuit connexion between the cortex and the thalamus explains that personality alterations can be achieved by ablating cortex, operating on the thalamus, or by cutting connexions between the thalamus and cortex. To achieve therapeutic results it will be necessary to remove a certain amount of cortex or to interrupt a certain amount of cortical thalamic connexions. If not enough pathways are cut or not enough cortex is detached, no improvement will result. If too much is damaged, rather marked personality damages are produced. We do not want to convey the idea that other factors do not enter in causing personality changes. The previous personality organization is certainly of importance. Nevertheless, we believe that the quantitative factor, especially in relation to pathway connexions should be carefully studied and evaluated.

Mentally well-integrated individuals who undergo frontal lobotomy are those who suffer from intractable pain. This case material is, however, not fully comparable to lobotomized mental patients because the operation is usually only performed unilaterally. However, in some cases bilateral lobotomy was performed and this was then used as a comparison. In these intractable pain patients the following was observed after lobotomy with individual variations: (1) Intellectual impairment is not demonstrated. All psychological tests indicate the same. It has not yet been reliably ascertained if the psychological faculties of superior intellectual functioning like creativeness, planning, etc., are interfered with. (2) A certain complacency is noticed. (3) There is reduced vivacity. Some patients appear to be emotionally dulled or flattened. A reduced alertness under ego involvement is noticeable which has two parts: (*a*) That the patient's anticipation of what will happen next is diminished; and (*b*) the evaluation of body sensations is reduced. Hypochondriacal preoccupations are markedly diminished. The alteration in the pain experience, however, is the most important one. Formerly the pain dominated the patient. It intruded into everything –

how he felt, thought, or what he contemplated. After the operation he may still be aware of the pain if he turns his attention to it, but ordinarily it is so undemanding that it can be neglected.

Formerly psychophysiological evaluations stressed the importance of the sensory perception *per se*. If we block or reduce the flow of sensory impulses to the brain, the pain disappears. Sedation accomplishes the same by dulling the perception. Nevertheless, the awareness and the concern over its source remain. Under opiates, for instance, even though the pain is diminished, the anticipation that the action of the drug will wear off remains and the concern for the origin of the illness is constantly present. With the use of intravenous sodium amytal the situation is different and has been observed to be similar to cases undergoing frontal lobotomy. The patient becomes unconcerned and quite relaxed. The anxiety which is so clearly mixed with the pain experience is gone. The pain perception is, however, not present as it is after lobotomy. They are not only unconcerned about pain, but they state that they do not have it. Deep hypnosis is able to produce similar alterations in pain perception like amytal by dissociating the whole pain experience from awareness.

We have to conclude from all these observations that we have a primary post-operative awareness of sensory stimuli and a secondary integrative awareness which incorporates sensory stimuli into the ego. This is a peculiar assimilating and detaching function. The ego registers the stimulus and then responds to it. This response can intensify the original stimulus or reduce it. This function of the ego is not that of permitting or not permitting the entrance of the perception into consciousness, but after it has permitted its entrance and recognized it, it does not acknowledge its importance. Sensory stimuli are, therefore, not simply perceived, but another more complicated and not yet fully understood mental process of attachment or detachment modifies the primary sensory perception into a secondary awareness of caring or not caring. Quite often these patients state they still have the pain, but they do not act like persons who have it. It is not yet clear if the quantity of the stimuli received from the periphery is related to the extent of the lobotomy or not.

We believe that the observations made on cases with intractable pain give us a clue to changes seen in mental patients who have undergone frontal lobotomy. It is generally agreed, too, that certain abnormal mental manifestations like phobias, obsessions, hallucinations, and delusional experiences are best influenced. The patient's behavior towards his symptoms is very similar to that observed in pain patients. At first they are dominated by the symptoms, the ego is defenseless, and overpowered. The repetitive obsessive nature of such experiences is well known. After the operation all the symptoms are still present, but the attitude of the patient toward his symptoms has changed. He still has them, but he is not dominated by them and is able to live with their existence. It is important to point out that as far as we know today, based on inadequate follow-up studies, the basic structure of the neuroses and psychoses remains unchanged. Some patients who underwent psychosurgery show in general after operation unchanged dynamics. The retention of basic psychodynamic structures is clearly seen in schizophrenic patients. But even though the basic structure is apparently unchanged marked alterations are seen in the patient's behavior. His ego defenses are definitely lowered, the patient is not afraid, not self-conscious, contact with the environment is readily made, the tendency to self-evaluation in relationship to social anxiety is gone. Patients who were blocked in psycho-analysis in associating traumatic material now do it quite easily. It is especially striking to see that anticipation of failure is not entertained. The patient is hopeful of mastering previously defeating situations or he accepts personality defects and is not upset by them. Repetitive dominance symptoms such as depressions, hallucinations, and delusions are diminished especially when they are evolved on the basis of inferiority feelings or feelings of non-performance. Disintegrative symptoms, however, are also influenced

if the operation does not come too late. The results in deteriorated schizophrenics are not impressive if one expects recovery. Deterioration is as formidable a barrier to the effectiveness of frontal lobotomy as it is to all other therapies.

We must also spend a little time on the personality damage problem which is an important part of the operative results. Intensive and extensive psychological investigations show practically nothing. This is as valid for intelligence tests as for performance, projective technique tests, and psychophysiological test situations. This does not mean that such a damage does not exist; it only indicates that our present methods of testing are too crude and new ones will have to be devised. The highest symbolic functions like planning, foresight, and creativeness which can be demonstrated clinically to be sometimes impaired do not show up in tests because we do not have tests which reliably demonstrate impairment in these mental functions.

Clinically, the most conspicuous damage is a certain inertia or apathy. The patient has no sustained effort, especially concerning intellectual performance, no drive to creative achievement, sublimated tendencies are impaired, there is very little anticipatory goal-setting present and no foresight. If the patient sets a goal for achievement, he does not use new methods for achieving it, but manipulates only the methods known to him (Halstead). The Gestalt configuration, however (in the sense of Goldstein), is intact. A 'don't care' attitude, day-to-day living in happy equanimity is present in many patients as seen similarly in primitives or children. The depth of emotional experience is reduced. Social sentiments are often also impaired by a careless and uninhibited behavior. The question arises – are these personality impairments, which, by the way, in a number of patients are not permanent, due to an organic brain damage *per se*, or are they the sequence of the elimination of anxiety, tension, and ego awareness? Both possibilities can be discussed. We believe that the second assumption is the more fruitful. Our society is built on a certain amount of anxiety. Without it, no socialization of the human being would be possible. All cultures have it to a varying degree. Anxiety is, therefore, used as an ego regulative function against other drives and if sublimated it performs as creative energy. If all tension and anxiety are cut and self-evaluation becomes indifferent to the individual, the setting of goals, plans, and anticipatory activities change into complacency. We believe that intelligence is utilized differently, whether such a driving force is present or not. It is logical to assume, therefore, that the elimination of anxiety and obsessiveness is inexorably connected with personality damage. However, this does not mean that extensive brain damage is absolutely necessary to achieve results even though some maintain this view. We do not know the optimum operation yet. It is possible, as some of the recovered cases indicated, that the operation balanced well between symptom reduction and damage. In most instances today we probably damage more than necessary. Our present methods of operation are still very crude and not reliable, but the question is open and will have to be investigated further.

Frontal lobotomy points to a very important problem in therapy. Most of our psychiatric treatments, and especially psychotherapeutic ones, mainly consider the qualitative approach to the disease. We try to find out by analysing the psychodynamic factors of the case: what conflicts in what constellations produce the emotional disorder. We overlook the fact that many of these conflicts can be present in a person, and he still does not show an emotional disease until the symptoms become so marked that he is obsessed by his fears or is dominated by his hallucinations and delusions. Therefore, we are dealing here with a quantitative treatment which leaves many of the underlying conflicts unimpaired, but somehow the patient does not perceive the conflicts any more and is not disorganized by them, permitting him to function. We believe that this quantitative aspect of the symptom in an emotional disorder is of great importance and will have to be studied in detail, particularly in relation to the quantitative aspects of the problem.

With the present state of our knowledge it is not possible to decide exactly what kind of patient should receive what kind of operation. The selection of patients today is mostly based on technical preferences and not on clinical symptomatology. Therefore, in some clinics all patients are subjected to a translateral form of lobotomy, others to a topectomy, or cortical undercutting, and again others to transorbital lobotomy. We believe, however, that besides the technical surgical issues involved, we must investigate which operation benefits a certain type of patient most.

In this respect, not too much is known. It was felt by some that catatonic patients responded better to operations which cut the upper quadrants, and still others maintained that delusional and obsessional patients fared better by cutting the lower quadrants. In our experience these observations cannot be confirmed. On the other hand, it can be confirmed that aggressive, destructive patients benefit more by operation performed more posteriorly. Aggressive, destructive patients therefore fare better with the classical form of lobotomy than with topectomy, or with cortical undercutting which is, by the nature of the operation, always performed frontally.

Seemingly there is no special relationship between the mental disorder from which the patient suffers and the type of operation the patient should have. It is not too important if the depressive, obsessive, or schizophrenic patient receives translateral lobotomy, topectomy, or any of the other operations. There is also (seemingly) no convincing evidence that a relationship exists between special clinical symptomatology like anxiety and obsessiveness and a certain type of operation.

In most operations performed, it is claimed that the same set of clinical symptoms are influenced by them. Patients suffering from a tension, obsessive-compulsive or phobic symptomatology benefit most by the operation. Hallucinations and delusions are also influenced if tension symptoms are present in connexion. Apathetic, driveless patients do not often benefit much by the operation. Deteriorated, schizophrenic patients respond best to the more extensive operations even though the improvement is often only palliative. Transorbital lobotomy does not affect deteriorated patients very much. Occasionally, however, we have even seen schizophrenic patients who appeared to be deteriorated and who responded to transorbital lobotomy. It is possible that these patients were only regressed and not deteriorated. The differentiation between regression and deterioration is not always clear cut and it is therefore possible that improvement is sometimes reported with deteriorated patients.

We have to evaluate the different operations also from the point of view of personality damage which is a very important feature of psychosurgery. In this respect, the ideal operation would be the transorbital lobotomy in all patients because the personality damage is nil or minimal. However, all the major operations often produce personality damage. The only question is: Do they all produce damage to the same extent? Here we believe that of the major operations the most extensive personality damage is produced by the translateral lobotomy. The damage is less extensive with the cortical operations like undercutting and topectomy. We have no figures on thalamotomy.

Today we use the following indications for operations: With well-preserved, not deteriorated, patients, who have been sick for only a year or two and who have not responded to shock treatment and psychotherapy, we suggest a transorbital lobotomy with an extensive frontal cut. With patients who have been sick three or more years, we suggest topectomy or cortical undercutting provided the patient does not show aggressive, destructive behavior. If they did, we would suggest the translateral form of lobotomy. In deteriorated, schizophrenic patients we suggest always a major operation like topectomy, undercutting, or the translateral form of lobotomy. We do not suggest the transorbital form of lobotomy because it is not sufficient to influence deteriorated symptomatology.

In the appraisal of the results with psychosurgery, we will have to differentiate more

sharply than has been done until now between a curative improvement and what we call a palliative one. In patients where we are able to eliminate the psychoses as in chronic depressions, or in some obsessive compulsive neurotics whom we can relieve completely from suffering, we could speak about a curative result. The same can be said on the outcome of the operation in some schizophrenic patients. It is obvious, however, that if we call the above-mentioned patients cured, they should not show any marked personality damage. If they do, we have relieved them from their suffering but inflicted a certain damage as payment for it.

In the majority of the patients who were operated, and this is especially true for the large number of schizophrenic patients, we cannot speak about a curative effect of the operation because it does not remove the patient's symptoms all around, but only palliates some symptoms, relieves, or alters some features of the psychosis. These schizophrenic patients often remain basically as schizophrenic as before the operation, only the impact of some of the symptoms, for instance the hallucinations and delusions, is markedly lessened. Usually they do not display as much aggression and appear to be happier because their tension is reduced. These patients then are able to live outside of a hospital and are even able to indulge in some work. However, they cannot, from a clinical psychiatric point of view, be considered cured. We do not want to minimize the importance of this symptomatological improvement, but on the other hand, we should not confuse it with the real cures; otherwise, psychosurgery would soon be discredited in the minds of those who are not able to differentiate between these two aspects of improvement.

THEORETICAL AND CLINICAL CONSIDERATIONS OF VARIOUS LEUCOTOMY TECHNIQUES

By Professor WALTER FREEMAN, M.D., Ph.D.

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Safety and effectiveness are the two main considerations in choosing an operation for the relief of mental disorder, but accuracy is coming to be an important feature, and availability is also stressed in view of the large number of patients that are being considered for psychosurgery. Since leucotomy can relieve the distress connected with terminal carcinoma and similar unbearable pains [1] the general surgeon as well as the psychiatrist should share in the doctor's outstanding contribution to human welfare, namely, the elimination of suffering. Transorbital leucotomy [2] is within the capacity of the psychiatrist.

Safety has already been achieved in large measure. The various operations upon the frontal lobes have never killed as high as 10% of patients in any considerable series, and usually the mortality has been maintained around 3%, while some teams boast 1%, or less.

Effectiveness is largely dependent upon the psychiatrist. Brazilian psychiatrists [3] apologize for their poor results, stating that only the most chronic and deteriorated patients were operated upon. The Board of Control [4] found a direct relationship between duration of psychosis and result.

Freeman and Watts [5] stressed the need for accuracy in the placement of the incisions and Alfred Meyer [6] has described the variability of the incisions found in his pathological material. If neuro-anatomy means anything, it is certain that symmetrical parts of the brain exercise similar or complementary functions. As far as leucotomy is concerned, the effect of operation is due to two factors, the mass of

tissue inactivated, and the specific areas of the thalamus that undergo retrograde degeneration. Thus, a large frontal lobectomy or an extensive leucotomy limited to one side will produce effects upon the personality that are quite definite although usually only temporary. The therapeutic effectiveness of unilateral leucotomy in mental disorders has been overstressed [7]. Asymmetrical bifrontal leucotomies, which make up some 90% of the case material in most anatomic series, are effective, in that both sides have certain symmetrical regions cut off from the thalamus.

Topectomy [8] has brought precision to operations upon the frontal lobes, in that symmetrical areas have been removed. Painstaking operations by the precision method of Freeman and Watts [5] with roentgenographic verification have enabled surgeons to approach the ideal of accuracy. However, the extent of operation as well as the plane in which it is done, is presumably important, and accuracy in this regard has not yet been achieved. Incisions in one hemisphere are apt to be different in their completeness even though carried out in the same plane. The retrograde lesions of the thalamus are consequently asymmetrical. This may be of minor importance. The social effectiveness of the patient necessarily depends upon the reorganization of the frontal lobe tissue remaining after operation. In a few of the Freeman and Watts series where asymmetrical lesions were evident in roentgenograms, the impression was gained that the operation was as effective as could be expected from the incisions made in the hemisphere with the anteriorly placed incisions. Revision of operation in a few cases was limited to the part of the frontal lobe not disconnected, and sometimes the results were satisfactory.

Availability of operation to large numbers of patients demands simplicity. Thalamotomy [9], cortical undercutting [10], topectomy, and even precision leucotomy are beyond the powers of all but the neurosurgical team. Frontal leucotomy by either the open [11] or closed method is within the capacity of the general surgeon, and should be more widely used for the relief of suffering in terminal carcinoma. Transorbital lobotomy [2] brings psychosurgery within the field of the psychiatrist. A recent letter from C. L. Jackson of Rusk, Texas, some two hundred miles from the nearest medical center, reports 400 patients operated upon in eight months with three deaths and 20% of the patients out of the hospital. Most of these patients were of the chronically disturbed type.

The topectomy research [12] has shown that most leucotomies are unnecessarily extensive. Better results are achieved with removals limited to areas 9 and 10 of Brodmann. Certain patients recover more satisfactorily after surgical lesions limited to the orbital quadrants [13], and the selective leucotomy [14] used largely in England is also proving the value of limited operations. Personality down-grading is highly correlated with the amount of frontal lobe disconnected. Other factors being equal it is possible to predict the social effectiveness of the leucotomized individual by studying in the roentgenogram the location of the incisions in relation to the coronal suture and sphenoidal ridge.

Freeman and Watts [15] have studied the plane of section in relation to social effectiveness. Incisions made 10 mm. behind the sphenoidal ridge will, in most instances, relieve a severe chronic psychosis and will enable the individual to engage in a simple occupation. Incisions 15 mm. or more behind the sphenoidal ridge result in helpless invalidism. Incisions anterior to the sphenoidal ridge permit the patient, if relieved of his psychosis, to engage in constructive work, and also to enjoy active recreational, social and intellectual pursuits.

Examples of creative activity, except for the "creative spell" as described by Reitman [16], are rare, even with the most anterior incisions represented by topectomy and transorbital leucotomy. There would thus appear to be a certain hierarchy of frontal lobe functions ranging from the simplest learned motor patterns, to the highest creative flights of fancy, and ranging also from the simplest aspects of visceral sensi-

bility through the development of personal and social self-consciousness to a certain spiritual self-consciousness with culmination in fantasy and ecstasy. The farther back one cuts, the greater the loss of these higher functions.

Psychological Tests and Psychosurgery

The tests used in leucotomy studies have been insensitive to all but the grossest disturbances of personality. The losses observed soon after operation are made up in the ensuing months. These losses are apparently non-specific, and merely reflect the general damage to the brain. There is an extraordinary spread between the intelligence test scores and the individual performance of the patient in his social situation. Given a task, the well-preserved patient can perform as well as his relatives, or even the psychologist's relatives, yet the patient is woefully lacking in the ability to erect his own problems and seek their solution. The frontal lobes are apparently necessary to enable the patient to climb out of his rut and find out what is going on in the world. The leucotomized patient is, to a greater or lesser degree, lacking in intellectual curiosity. In this situation the psychological tests are reminiscent of the animal acts at the circus.

Psychological tests have been devised by Mary Frances Robinson [17] to measure the interest that the patient has in himself, since the self looms so large in any consideration of psychosis and psychosurgery. The problem was formulated in the following way: Get the patient to talk about himself and find out how long he can continue. Dr Robinson spent a year in Washington and is continuing in St Joseph, Missouri. There is a high and inverse correlation between the extent of the operation and the length of time a patient will spend describing himself. Table I gives the Self-Regarding Span (SRS) results:

Table I. – Self-regarding Span in Relation to Leucotomy

	Mins.	Secs.
Recovered without operation	8	27
Transorbital leucotomy	7	47
Minimal leucotomy (orbital only)	4	6
Standard leucotomy (coronal plane)	3	42
Radical leucotomy (10 mm. behind)	2	40

Robinson also devoted considerable time and effort to the development of a Sensibility Questionnaire in order to ascertain the degree of concern manifested by the individual for the opinion of other people and for his own past and future. Again, the results allowed some estimate of the functions of the frontal lobe. Maximum possible scores range from plus 20 to minus 20. Normal is balanced at zero.

Table II. – Sensibility Questionnaire in Relation to Leucotomy

Recovered without operation	+ 9·4
Transorbital leucotomy	− 4·4
Minimal leucotomy (orbital only)	− 7·5
Standard leucotomy (coronal plane)	− 9·4
Radical leucotomy (10 mm. behind)	−12·3

It may be seen from these tables that following leucotomy there is reduction in preoccupation with the self, and even more so in a certain recognition of the self in relation to the social environment. Leucotomy effects a specific reduction in the individual's feeling of self-continuity.

Lidz [18] has stated this in almost epigrammatic fashion. 'Even as anxiety is absent without anticipation, depression may well depend upon an appreciation of the past. Without ability to compare the present and future with past experience, brooding disappears.'

From the clinical standpoint, the operation of leucotomy should be adapted to the needs of the patient. An inadequate operation is useless; a too extensive operation is crippling. Granted that the patient has not deteriorated beyond recall, in which

case no operation should be performed, the leucotomy should be just sufficient to relieve the neurotic or psychotic preoccupation with the self, without at the same time trespassing upon those parts of the frontal lobe that are necessary for adequate social reintegration. The goal of 80% is not too high.

SUMMARY

The prime considerations of safety and effectiveness of frontal leucotomy and related operations have been achieved. Accuracy and availability to large numbers of psychotic patients are desiderata. The operation chosen should accomplish its task without damage to the patient's ability to adjust himself in society.

There is a direct relationship between the plane of the leucotomy incisions and the social effectiveness of the individual. Provided the psychosis is relieved, the further anterior the incisions are made, the more effective will be the social adjustment. Psychological tests reveal that the plane of section affects the individual quantitatively in his self-regarding span and in his sense of self-continuity. Most leucotomies have been unnecessarily extensive.

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REHABILITATION AFTER LEUCOTOMY

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One thing that has become evident in psychiatric therapy is that no single treatment is a specific. The same principle obtains in the operative sphere of leucotomy. Leucotomy has proven to be somewhat like shock therapy in that it 'clears the decks' for the construction of a more adequate personality, but the operation leaves an even more malleable personality than does shock therapy.

Our first leucotomy at the Institute of Living dates back to 1938, and we have found many factors in the post-leucotomy personality that demand the immediate application of a post-operative rehabilitation program; this in the emotionally-neutral hospital atmosphere, but to a considerable extent separate from the regular hospital program.

Surprisingly enough, post-operative rehabilitation has received very little space in the literature. I have found no writings devoted especially to the subject, which as a rule in psychosurgical articles has been limited to one or two statements to the effect that immediate psychiatric re-education following the operation is most important.

At the Institute of Living, we have found that following the operation, we are usually dealing with a 'third personality' – different not only from the psychotic or psycho-neurotic personality, with all of its emotional stumbling blocks, *but also* different from the pre-psychotic personality, which succumbed in the first place.

In general, we may say that the leucotomized personality is compounded of reduced affectivity and increased responsiveness to immediate stimuli and environment. Intermingled in this 'third personality' is a large part of the pre-psychotic personality, as well as varying amounts of the psychotic personality.

From a re-educational standpoint, perhaps the most outstanding characteristic of a post-leucotomy personality is a greater susceptibility to the external environment. This environmental susceptibility is usually most striking immediately following the operation, which gives us a key to the fact that this is probably the optimal time to launch the patient on an organized program of re-training and re-education.

There is some difference of opinion in this matter, however. Some feel, for instance, that at this stage the patient should be returned without delay to the community or the home. I personally would certainly prefer to send the patient home if the only other alternative is to return him to the psychotic groups within the hospital, but the question should be raised here as to whether or not we should take a chance on subjecting the patient to the highly uncertain circumstances within the home, i.e. the many factors associated with the variable degree of tolerance on the part of family and friends towards the patient's unusual conduct immediately after the operation.

It seems to me that since the precipitating factors of the illness may be, in part, in the community, it is an obvious risk to jettison the patient back into the explosive situation without first teaching him to cope with the circumstances. This is particularly true when the precipitating factors are contained in family conflicts and tensions.

For that matter, experience has taught us that some patients, even with and after their re-training, should never return home. We have had many patients who, in spite of good progress at the hospital, encountered difficulties on trial visits home, but made good adjustments when they were placed in jobs away from home and family.

Oftentimes, if not usually, the family is unable or unprepared to accept the responsibility of the post-operative care and training. As with many psychiatric patients, it is usually necessary, but sometimes impracticable or even impossible, to re-educate the family in its attitudes and reactions and to teach the members to become accustomed to the patient with the modifications and limitations that are sometimes present.

One of the many cases in my experience that illustrate this point was an 18-year-old youth who had been diagnosed as an encephalitic at the age of 18 months. Subsequently, he had been an abnormal child presenting behavior problems, and he had lapsed finally into the psychotic stage, spending a great deal of time in institutions, where he had been assaultive, destructive, and extremely antagonistic toward his parents and his doctors.

After his leucotomy, he had no memory or feeling of antagonism, but he presented post-operative symptoms of slowness and incontinence. Nevertheless, he was progressing nicely when one day his mother visited him. She, a highly emotional, tense person, became extremely distressed at his slowness; she exerted a most disturbing effect on the patient; and she ended up hysterical in the doctor's office. There it was explained to her that her son was going through a temporary phase, and after considerable persuasion, she agreed to discontinue her visits for a time.

During the next three or four months, with intensive re-education, the patient gradually grasped his surroundings and his initiative increased. Five months after the operation, he spent some time under supervision at the family summer home on a trial basis. This trial visit, however, turned out to be a failure, with the result that the patient returned to us with a recurrence of his symptoms. Then and only then were we able to persuade the family that the home, and especially the mother, were bad medicine for this young man. After remaining with us for a few more months, during which improvement ensued, he has since been permanently established away from his family outside the institution.

The point in question is that this patient's increased post-operative susceptibility to his environment was a weak point at home, whereas in the hospital, under the proper stimuli and guidance, it was utilized constructively. We have ample reason to believe that if he had returned home permanently, the results of the operation would have been predestined to be a failure. As it was, he has returned to society on an independent basis.

Granted that hospital re-education is called for, the question naturally arises as to where in the hospital the post-operative patients should be domiciled and re-trained. Although one group has published the opinion that a segregated post-leucotomy program within the hospital has no particular advantages, we have found at the Institute that a separate program is in the best interests of *all patients in residence*.

On the one hand, leucotomy patients do not fit well into the regular convalescent groups. They exert a disturbing influence on convalescent patients because of surgically-induced symptoms – impatience, impulsiveness, irritability, lack of initiative, poor personal habits of eating, dressing, etc.

On the other hand, placing post-leucotomy patients with the regular psychotic groups was also found to be inadvisable. If placed with psychotics, they tend to perpetuate their own psychotic patterns, more particularly in the area of behavior and sometimes in their delusional content.

In a sense, post-operative patients are reminiscent of a parrot; with their increased susceptibility to their surroundings, they tend to pick up behavior eccentricities or bizarre delusions. These they interweave in their own patterns, ending up with the total amount of their pathological behavior and psychopathology increased.

In other words, the post-leucotomy patient is bad for the convalescent, so administratively he belongs with the psychotics, but placing him with the psychotics militates against his own recovery.

Somewhat reluctantly – in part because of administrative difficulties, and also because of the initial financial outlay – we were forced to the conclusion that if we were to continue serving the psychotic through psychosurgical procedures, we had to establish a service that would be devoted primarily to post-operative care and training.

As a result we have developed at the Institute a complete and independent service that is now housed in its own structure. Residential quarters for these patients, a specially planned operating suite with provision for teaching facilities for the profession, a recovery floor and a floor of classrooms and other post-operative training facilities are all under one roof. This set-up, dedicated exclusively to this group, seems to have gone a long way toward solving the problem.

The candidate for operation, who is moved to this unit only immediately before operation, is placed upon the operative recovery floor. After the operation he is returned to this floor and his program of re-education is promptly started. Preferably the same day, and in any event, as quickly as possible, he is entered in the special leucotomy classes, which I shall describe later. If success crowns our efforts, the post-leucotomy patient is eventually transferred to a regular convalescent unit, where he mingles with all other convalescents.

Along with his latter move he may be granted a series of graduated privilege cards, the first card placing upon him the responsibility for going unescorted from convalescent class to convalescent class and back to his residence. The next card allows him freedom of the campus until six in the evening, and then until nine. Still further privilege cards extend his activities to the city of Hartford, and even to the State of Connecticut.

By this time, it has been amply demonstrated whether or not the patient is going to be assimilated into society, and we have had the opportunity to iron out any difficulties that may have arisen. There has been no sudden move or jump. To all practical purposes the patient has been insinuated into society.

I would not have you believe that this technique is always followed, but it is our objective and it is carried out to the extent that the family and other circumstances permit us to do so.

In the program just described, between 30 and 40 post-leucotomy trainees are carried at the Institute at one time. Of this group, between 20 and 30 are in the special training program, while a handful are not yet ready to participate, and still others are with the regular convalescents and are about ready for ultimate departure from the hospital.

We have found it advisable to keep all post-leucotomy patients in the hospital for a time after the operation, regardless of how much improved they may seem to be.

Although some patients appear well immediately after the operation, we have often observed a marked discrepancy between their superficial behavior and the findings of Rorschach tests which continue for some time to show evidence of pre-operative abnormal personality function.

For example, we had one patient, a successful architect, who for ten years had suffered from persistent, disabling hallucinations and delusions in every sensory modality. One of his most common experiences would occur when he took a pencil in hand. 'They grab it from me and won't let me work', he told his doctor.

While he had no insight whatsoever, he maintained the intactness of his personality – that is, his delusions stopped short of affecting the rest of his reasoning; he had a good appearance and behavior, and unless he told you of his symptoms, you would have had no hint of them. However, his difficulties had interfered with his vocation, and alcohol had become a problem.

During the ten years he had been ill, he had submitted to repeated therapeutic efforts. He had spent a year being psycho-analysed and, when that failed, he had gone to one of the leading shock men for insulin and electric shock therapy. Finally, leucotomy was undertaken as a last resort.

He appeared perfectly well the third day after his operation. He denied all of his symptoms. His I.Q. and C.Q. checked well; as a matter of fact, he recorded an I.Q. of 125; but his Rorschach gave him away – for some time it showed evidence of his illness.

It was an interesting phenomenon that during the following weeks he never mentioned his symptoms voluntarily and, except when asked insistently, he would not admit that he was still occasionally troubled. Only with time, re-education and psychotherapy did his symptoms disappear entirely, and he has now resumed a highly successful career.

This architect might be compared to certain cases of atypical virus pneumonia that were experienced in the army during the last war. These cases are reported to have shown minor outer symptoms of a slight fever or cough, with x-rays revealing marked clouding of the lungs. In a week, the patients were inclined to 'feel fine', their fever and cough were gone, and they were reluctant to stay in bed.

However, their x-rays continued to show a pathological condition of the lungs for two to four months, and it was learned through experience that these patients should be kept in bed until their x-rays cleared. When they were allowed up before their x-rays cleared, complications, sometimes more serious than the initial ones, tended to arise.

The Rorschach evidence of leucotomy patients, like the x-ray of the virus pneumonia patients, may show a basic pathology; and we have learned that it is important not to overload the patient prematurely with emotional stress and strain, but to keep working on the situation in a protected environment.

Such is not always the case. One of our most remarkable recoveries was a middle-aged woman who had been hospitalized twice previously with a severe depression. Actively suicidal, she did not get well or stay well with shock therapy, and it had been a serious problem to keep her alive.

Within six weeks after her leucotomy, she had improved so much that both she and her husband insisted she was ready to go home. She looked and acted as if she were, but we did not trust the depth of her improvement. However, personality studies, twenty-four-hour-a-day observations, and penetrating interviews failed to disclose any remnant of her difficulties.

A little more than two months after her operation she went home on trial visits, during which she attended parties and also entertained in her home. She has now been discharged, and there has been no recurrence of her depression whatsoever.

So it is that with the leucotomized personality, we are dealing occasionally with patients who make a spontaneous recovery, but these are the exception rather than the rule; we are dealing sometimes with patients who only apparently have made a spontaneous recovery, but who actually have persisting underlying abnormal personality functions that require special understanding and handling; and we are dealing sometimes with patients in whom the need for special attention is outwardly apparent to the doctor and even to the family.

Our job post-operatively is to determine to the best of our ability the patient's exact and actual condition, and then to provide the environment, the guidance, and the training that will best prepare him to function as a more successful enduring member of society. In this endeavor, for the reasons I have just outlined, I believe that the post-operative rehabilitation program is an essential vehicle.

We cannot emphasize too strongly the importance of the patient getting promptly into post-operative activities in order to take full advantage of his highest degree of responsiveness and also to prevent his slipping back into psychotic patterns.

We have found that one of the most important realizations of the rehabilitation program is re-socialization. As we all know, with mental illness, we are often dealing basically with problems of interpersonal relationships, sometimes problems involving numbers of people, and sometimes involving only members of the opposite sex.

After leucotomy, patients are often still inclined to lack the confidence and stability for adequate interpersonal relationships. Further, they are commonly less aware of the feelings of others, are more or less tactless and rude, and unobserving of the social amenities.

Because adjustment to both sexes is so important in our society, and because it is essential that the leucotomy patient be exposed post-operatively to an environment patterned after the normal, all of our post-leucotomy activities, except sewing, woodwork, and so forth, are for men and women together. It is a controlled situation;

as soon as a patient is able, within seventy-two hours and sometimes the next day after the operation, he is scheduled for group activities. If he *cannot* make the grade, he is taken out of the group and returned when improvement ensues. A daily social hour has proven particularly effective.

One of the most striking examples of this need for re-socialization is a young man who had always had difficulty in adjusting to the opposite sex, although he got along fairly well with men. Pre-operatively and immediately post-operatively, he was inclined to strike women, spit at them, use foul language, and in general behave in a highly objectionable manner.

For some months post-operatively he progressed in all respects except this one. But gradually, and carefully, he was introduced to the social hour and it is a source of considerable satisfaction to us that he is now dancing and acquiring quite a polished manner with members of the fair sex.

We also had a woman in whose illness the precipitating factor had been an unfortunate love affair. Pre-operatively and post-operatively she was viciously antagonistic towards all men, but much the same thing has been accomplished with her as with the young man.

In both instances, it is doubtful that re-socialization would have been spontaneously accomplished merely by sending these patients home or allowing them to follow their own bent. Also, I would like to emphasize that they would have been rejected by the convalescent groups, and their old disability would probably have been perpetuated if their social re-training had been undertaken in the midst of the psychotics.

Another important feature of the post-operative rehabilitation program is constant guidance and drill in matters of good personal hygiene, which in many instances the home does not provide. Families seldom use the correct techniques for re-training, or they find these techniques to be so onerous that often they finally abandon the entire program altogether.

Additionally, inquiries have revealed that training along these lines, when undertaken by us, does not result in personal conflicts that so often arise in the home. All of us are inclined to accept correction more gracefully from neutral persons than from certain members of our family, and there is nothing about the leucotomy patient that lessens this natural tendency. As a matter of fact, the operation probably increases it, as expressions of resentment, which require careful handling, are a common feature in the post-leucotomy picture.

Vocational training is also included in our program, and a very important part it is. We have found post-leucotomy patients to suffer more from 'loafer's delight' than almost any other group of patients at the Institute. As a result, they need more prodding and individual attention, but if we are truly trying to reassimilate these patients into society, we most do so in terms of their carrying some responsibility outside the hospital. This is best expressed by the term, 'vocational responsibility', be it as a housewife, or an accountant, or a labourer.

Before each operation, an estimate is made of the patient's vocational potentials when and if we succeed in establishing him outside the hospital. Preferably his vocational program is not only envisaged but is actually planned and started before the operation. It is persisted in with the aim in view of having the patient leave the hospital to go into responsibility without any vacation or any rest period.

My own experience and belief are that if we in society have a reasonable vocational anchor, the social amenities and other factors in our emotional adjustment are more likely to take care of themselves. If there is no anchor, the old adage, 'Satan finds some mischief still for idle hands to do', has a therapeutic significance, and that remark is not just a nursery adage.

Finally, our program provides for avocational training. Every person needs an

avocation or hobby to absorb the skills and vocational urges for which society has no use, and the leucotomy patient, more than the average, must have his hobby or avocational potentials thought out and developed.

These hobbies must be developed at least in an embryonic form, during the post-leucotomy training program, with the environment to which the patient is returning being kept well in mind. It is useless to talk of gardening as an avocation for an Eskimo, or of raising puppies as a hobby for a person who must live in a New York apartment. Hobbies that will persist into the post-hospital period are the only ones that have any enduring value whatsoever.

Our findings in the sphere of intellect, imagination and initiative have been very interesting and encouraging. Although with our present knowledge it is early to say, our experience indicates that while the operation reduces the number of association pathways, it does not necessarily interfere permanently with intellect, initiative, and imagination.

A battery of tests, administered at frequent intervals by a Ph.D. who is devoting full time to pre-operative and post-operative studies, show in the majority of cases a progressive post-operative increase in intellectual functioning level to normal. This is often above the psychotic level, as with the architect we have just mentioned.

This also holds true with an interior decorator who for years had recurrently been deluded, persecutory, actively suicidal and unable during these times to pursue her occupation. Leucotomy procured for her better and certainly more enduring improvement than either electric or insulin shock therapy.

I recall that during her hospitalization, her family home was redecorated, and, on one of her post-operative visits home, she is reported to have made an accurate criticism of the way it had been done. She is now living alone, away from her family, where there *are* difficulties, and she is successfully carrying on her profession with confidence, graciousness and poise – this after she had been hospitalized four times in the previous five years!

Our experience indicates that whether or not the average processes of intellect, imagination and initiative are 'normal' post-operatively depends largely on the original endowments of the patient and how much, if any, deterioration has set in. *Other factors*, such as innate incentives, acceptance of circumstances, and so forth, *are also undoubtedly important*, and these *can be developed* by immediate, intensive post-operative re-education and psychotherapy.

Incidentally, I would like to sound a warning against the too liberal use of the word 'deterioration', which only too often is more apparent than real. Often the so-called deteriorated patient *is merely desocialized* as a result of a protracted illness or hospitalization, and not deteriorated at all. To my way of thinking, these cases are the greatest existing challenge to our techniques of resocialization.

In the matter of *associating post-operative techniques* with the *different surgical procedures*, it has been our good fortune at the Institute of Living to have our own cases operated by top-flight neurosurgeons in the United States, and also to provide post-operative care for other cases who had been operated by men in various parts of Europe and North and South America. These men have used various techniques and have attacked different parts of the brain.

I wish we could identify the post-operative rehabilitation necessities with the different procedures such as the original closed technique; the Poppen-Lyerly open technique; the topectomy; the undercutting; and the transorbital.

Thus far, the re-training necessities of these different operations have not seemed to fall into any established pattern. Instead, they show extreme variability, and we have been unable to establish any particular advantages of one re-training procedure over the others in connexion with the various operations.

If we could state in advance that these are the re-training necessities and potentialities

for that operation, we would have taken a considerable step forward. However, up to this time, all we can state with absolute certainty is that some manner of re-training is necessary to the maximum success of the operation.

In conclusion, let me state that the basis for developing this re-training program was the assumption that the illness produces certain habit patterns that tend to persist into the post-operative period; *further*, that an organized effort to break up these patterns and to substitute healthy patterns must have some advantage over leaving the matter to chance; and *finally*, that the exposure to normal, or at least near-normal, environment is essential to any reasonable degree of success.

It is far too early to make any dogmatic claims, but I feel that our post-operative rehabilitation efforts have played a leading part in the success of our psychosurgical endeavors.

Discussion

Professor Alfred Meyer said that while he greatly appreciated the honour of being asked to open the discussion on these stimulating papers, he felt he must emphasize that his competence to do so was strictly limited to a few theoretical aspects because his and his associates' experience at the Maudsley Hospital had been confined to investigations which were primarily anatomical. They had led to certain clinical correlations but the starting point was anatomical.

One point which struck him very forcibly during the evaluation of results was the linkage between personality change and improvement. Personality changes were sometimes spoken of in the meetings as undesirable and avoidable sequelæ of the operation and it was not always realized that they were essential for improvement; this had also been emphasized recently by Mayer-Gross and Frankl. This did not mean, of course, that the greater the personality change, the greater will be the improvement; it meant that the personality change which should be aimed at in the operation should be sufficient to meet the requirements of the individual patient. In prognostically favourable cases even a slight personality change, e.g. a reduction of tension, would accomplish what was desired, but he doubted whether there would ever be an improvement without primary causation of personality changes.

One important result of his and his associates' studies was that the degree of personality change depended more on the amount of prefrontal tissue damaged than on the localization of special mental faculties in any specific cytoarchitectural area. There was a slight predominance of the orbital region with regard to personality change (not only of the euphoric type), but any specific localization which may exist is overshadowed by the quantitative principle. He was happy that Dr Scoville and Dr Hoch in their papers had fundamentally agreed with this (quantitative) view and he also thought that the theories of Dr Freeman and Dr Watts on frontal lobe function could – to a considerable extent at least – be reconciled with a quantitative principle.

It was rather unfortunate that cytoarchitectonics have been so closely associated with psychosurgery. The wider psychiatric public had been – rather unduly – impressed by the apparent accuracy of the cytoarchitectural map of Brodmann, von Economo and others and it was not sufficiently realized that these charts were based on the investigation of only a surprisingly small number of brains of primates including man. Lashley and Clark have recently drawn attention to this fact and – in macaques – they were able to demonstrate the doubtful validity of some of the frontal subdivisions emphasizing that the architectural differences were only slight and variable from individual to individual. The present speaker and his associates are engaged in work on the individual variability and extent of the prefrontal areas in the human brain. They hope that in this way data will be obtained which may prove of interest to neurosurgeons performing localized operations on the frontal lobe of mental patients.

The mechanism of the personality change and improvement is unknown. Freeman and Watts suggested that it was the interference with the thalamic frontal projection. It had also been suggested that, in addition, there was interference with other fibre systems such as the short and long association of fibres and the suppressor mechanisms in areas 8 and 24. Perhaps the experience of Spiegel and his associates with thalamotomy would soon provide more evidence on this question. Actually, they claimed that personality change was less in thalamotomy than in frontal lobotomy, but in a few personally observed cases in which accidentally the lesion was confined to bilateral sectioning of the thalamo-prefrontal bundle in the internal capsule, resulting in complete retrograde degeneration of the dorsomedial nucleus only, the personality change was quite considerable. Further experience with thalamotomized patients will throw more light on this question.

Mrs ASENATH PETRIE said that it might be of interest in view of some of the remarks which had been made by the speakers about psychological changes after leucotomy to describe very briefly an investigation which had been carried out at St George's Hospital, London. For the last three years every patient recommended for the standard type of 'blind' leucotomy at this hospital, had, at the suggestion of Dr Desmond Curran, been investigated on an extensive group of personality and intelligence tests. All the patients had been tested before the operation and re-tested three months after the operation, and again nine months after the operation. The neuro-surgeon throughout was Mr Wylie McKissock.

It was important to mention that these patients were severe neurotics, rather than psychotics and were remarkably accessible. Among the tests used were those which had been shown by Drs Eysenck, Himmelweit and herself, to differentiate the neurotic from the non-neurotic, and the introvert from the extrovert. Other tests were devised to measure changes reported in the literature.

The investigation was designed to test the hypotheses that the changes in personality after leucotomy involved a loss in special aspects of intelligence, a decrease in neuroticism, and a movement away from introversion towards the extrovert type of personality. By comparing the test results on 20 patients before and three months after the operation considerable support was found for these hypotheses. After nine months the changes which supported these hypotheses were even more striking.

If only those changes were considered which would occur less than one in 20 by chance, using Fisher's test, it was found that in the sphere of intelligence there was a particular loss in verbal as opposed to performance ability; there was increased difficulty in learning and generalization, and there was a loss in social attitudes not related to the immediate environment. These changes had been shown on the full Wechsler Scale, Porteous Mazes, and the revised Stanford Binet proverbs.

On the temperamental side, using those tests which differentiated between the neurotic and non-neurotic, a decrease in neuroticism was found. This was shown by a decrease in prestige suggestibility, higher scores on a test of manual dexterity, a smoother work curve, and a changed attitude in the patients towards themselves.

A decrease in introversion was shown by the following changes on tests which differentiated between introverts and extroverts:

(*a*) Marked tendency to go for speed rather than accuracy in both manual and mental tasks, i.e. they were quicker but made more mistakes.
(*b*) Loss in physical persistence.
(*c*) Lower perseveration scores on motor tests of perseveration.
(*d*) Decrease in self-blame associated with an increased tendency to blame the environment.
(*e*) Preoccupation with the present and future as opposed to the past.

(*f*) A greater reality adjustment in goal-setting behaviour.
(*g*) An increased liking for sex jokes as opposed to neutral humour.

All but a few of these changes were already noticeable three months after the operation. They were confirmed, and in some cases accentuated, nine months after the operation. In no case was the direction of the change reversed after the longer period.

Among points of general interest was that the standard leucotomy patients showed increased distractability after nine months. The patients showed a decreased critical attitude towards themselves and towards the use of language. People of superior intelligence stated, for example, that 'Brave' meant to show good taste; that 'Belfry' was an alcove in which bells lay ; that 'fur' was used as a wearing apparatus and that 'aseptic' meant god-like.

All these changes were found, it must be remembered, in a group of neurotic patients who had undergone leucotomy. In Mr Crown's investigation there was some indication that if these changes existed in psychotics who had undergone leucotomy, they were difficult to demonstrate.

The patients undergoing unilateral and bilateral rostral leucotomy were being submitted to an identical investigation. The number of patients completed so far was too small to report anything but very tentative impressions. There was, however, a distinct impression that the personality changes were less marked after rostral leucotomy than after the standard type of operation. In no case had the rostral patients misused language in the manner she (Mrs Petrie) had described, which was such a frequent finding after the standard type of operation.

Dr P. MACDONALD TOW said that Dr Paul Hoch had emphasized that the improvement in schizophrenia must be regarded as purely administrative and that in no sense could it be regarded as a cure. Would Dr Hoch agree with him in looking at it in a rather different light if he suggested that there was psychiatric improvement in the more narrow sense of the term, but that this was sometimes outbalanced by deterioration in the general social and civil aspects of personality? With regard to his point that in cases operated on for pain the impairment in creative ability and planning was seen in a pure setting, but was not so certainly evident in the mental patients, the speaker would add that he had examined a series of some 45 mental patients carefully selected from a very large number and had found that their general state of personality preservation had shown marked deterioration in both these aspects.

There was one point he would have liked to make with Dr Pool, and that was that in his total of some 52 cases it was disappointing to find only 2 obsessional cases. He took it that these new procedures were intended to hold out some hope of being able to operate in well-preserved sane patients, producing fairly specific removal of their symptoms without personality damage. Dr Pool did not give any details of the relative psychiatric recovery. It would be interesting to know whether in those 2 cases alone, and in some of the cases of the subsequent speakers, there was the usual disparity, say, between the disappearance of the tension which went with the obsessional symptoms and the disappearance of the cognitive aspect of the same symptoms.

One last point: he had had a long discussion with Dr Scoville in the interval and was interested that Dr Scoville tried to convince him that the personality deterioration in patients operated on for pain was considerably worse in some cases than the deterioration of personality in psychotics. He (the speaker) had been for some time trying to persuade people that the deterioration of personality suffered by well-preserved mental patients was considerably more than that suffered in the psychotics. So, with the surgeons, he found himself taking the opposite point of view; the surgeon saw more strikingly the deterioration he produced in a previously normal patient, whereas the psychiatrist saw this deterioration against the improvement which

occurred in the psychosis. Were the two points of view married by saying that there was almost always improvement in the psychosis and deterioration of personality, particularly the more refined social aspects, and that it was merely a question of balance – the narrow psychiatric improvement against the general or social personality change?

Dr E. STENGEL wished to report a few observations concerning epileptic manifestations following leucotomy. They were generally regarded as one of the complications which had to be accepted in brain injury and which could not teach us anything new. However, it seemed worth while to look at these cases more closely. He followed up 330 cases, mostly psychoses, operated on by the standard method between 1942 and 1947, 10·9% had epileptic fits at some time before the end of 1948. If those who had fits only within two weeks following the operation were deducted, the percentage was 9·4. Surprisingly, none of the last-mentioned group had so far had any further attacks. The percentage of schizophrenics with epileptic manifestations following the operation was markedly higher than the percentage of those operated on for affective psychoses, 14·5% against 8·4%; the proportion of male cases was markedly higher than that of the females. All the psychotic patients who had their first fit more than three years after the operation were schizophrenics. Half of the patients had had only one fit so far, and another quarter had not had more than five fits altogether. None of the cases with more frequent fits had improved to any marked degree. Unfortunately, no electro-encephalograph investigations could be carried out. Those observations required re-examination on a much larger material. They were of interest in view of Dr Denis Hill's findings on the electro-encephalogram in schizophrenics.

He would like to say a few words about the indications for leucotomy. Professor Freeman had called leucotomy 'a measure of desperation'. However, it seemed that the level of desperation varied a great deal from place to place. A strong psychosurgical bias seemed to lower the threshold of desperation considerably. He fully agreed with Dr Hoch that the various mental conditions which appeared to call for leucotomy needed to be redefined, otherwise it was impossible to evaluate and compare the results reported.

Dr PAUL H. HOCH, in reply to the discussion, said he would like to mention a few points. He discussed first Dr Meyer's remark that there was a relationship between brain damage and improvement. This was maintained by a number of investigators but actually depended to a great extent on what one understood by 'damage'. It was obvious that many patients, but not all, who underwent leucotomy suffered a certain amount of damage. This damage was essentially in the highest intellectual and affective spheres. It cannot be measured, and at present cannot be demonstrated well by psychological tests. It can only be shown clinically. Dr Hoch had observed a number of patients with high intellectual achievement before the operation and in these individuals there was an impairment in their creativeness. It was a question whether impairment of creativeness was always produced by the operation. This would have to be investigated further. The impairment of creativeness should not be confused with ordinary intellectual damage. Ordinary intellectual functions are sometimes damaged and sometimes improved. Removal of tension and anxiety may permit the patient to use his intelligence to better advantage. He did not believe that 'damage' such as reduced initiative, inertia, asocial and anti-social behavior were necessary by-products of an improvement. He believed that such gross personality defects could be avoided and operations devised which would have curative effects without damaging side-effects.

He again stressed that the basic structure of the neurosis and psychosis after operation remains the same even though anxiety, obsessiveness, hallucinations, delusions,

etc., are quantitatively markedly reduced and have even disappeared. His remarks concerning improvement in schizophrenia were probably misunderstood. He did not wish to minimize the improvement which leucotomy is able to accomplish in a deteriorated schizophrenic, but stressed that this so-called palliative improvement should not be confused with curative improvement. From the point of view of research and intellectual honesty, one must say that prefrontal leucotomy is not a cure for schizophrenia but that it is able to ameliorate many of the symptoms to such a degree that the patient is able to live a fairly successful life.

Dr FREEMAN, also in reply, said that he thought an inordinate amount of attention had been paid to psychological tests. A patient who had been in an institution for five, ten or twenty years had become accustomed to certain forms, certain rituals, certain activities which arose from the location in which he found himself, and there must have been certain differentiation in the activities of the neurons themselves. Granted that a patient after five or ten years of illness had developed these patterns one could not expect him to return to a pre-psychotic level of activity no matter what one did. There were a few who showed marked improvement. In the earlier cases before this structuralization had gone on to completion there were even more striking examples of return to a normal pattern of friendly competitive activity than one found in the patients who had been mentioned previously.

He did not like to be accused of being too quick to rush in to mutilate the frontal lobes but he thought with experience one could almost, when one saw the patient for the first time, predict whether the patient was going to respond to conservative treatment or not. He did not think psychiatrists should wait too long in their conservative treatment before giving the patient the advantage of the reconstruction of the personality which followed lobotomy.

Dr BURLINGAME emphasized the importance of a full programme of rehabilitation after these operations. He remembered a dog who had injured his left front paw and who had run on three legs. After the paw recovered he continued to run on three legs until he was taught to run on four legs once more!

[*September 13, 1949*]

THIRD SESSION

CHAIRMAN

Sir HENRY DALE, O.M., G.B.E., M.D., F.R.S.

(*President of the Society*)

RELATION OF LOBOTOMIES TO THE SHOCK THERAPIES

By LOTHAR B. KALINOSWKY, M.D.

During the last fifteen years psychiatry has been enriched by several important somatic treatment procedures which, in spite of their shortcomings, have revolutionized our approach to the treatment of mental illness. Each of these methods was based on certain clinical observations rather than on an understanding of the disorders treated. Only secondarily did their inventors explain them with theories which mostly turned out to be unfounded. Taking this into consideration it is even more surprising that these therapeutic methods were introduced quite independently from each other and that furthermore the clinical and theoretical basis claimed for them, differed so widely.

Frequently the new methods competed with each other, and attempts to integrate them were made slowly and somewhat reluctantly. Few psychiatrists engaged in work with one of the newer methods took an active interest in the development of the others. This explains some of the shortcomings in their broader application and delayed agreement on their respective indications.

Therefore, it seemed worthwhile to investigate their relation to each other, to outline their differences, to compare some of their clinical manifestations and, at the same time, to see how much such comparison may teach us regarding their mode of action. Since the normal way of finding treatments with a rationale based on the etiology of the disease thus far failed in large groups of psychiatric disorders, one may hope that perhaps the knowledge acquired from the effect of new treatments will, some future day, contribute to the understanding of the diseases treated. If at the moment, such hope does not look too promising the approach tried in this paper might at least bring up a number of problems for discussion, and, last not least, give me an opportunity to present my practical and theoretical ideas on shock treatments and psychosurgery.

It is true that all shock as well as psychosurgical methods were originally recommended for the large disease entity of Schizophrenia, where they still find their widest application. But when we are confronted with an individual case, indications for shock and psychosurgical procedures do not overlap as often as could be expected. In most cases shock treatments should be applied to the utmost before surgery can be considered. In many others, though, shock therapy is hardly promising or not even indicated. Selection of patients for psychosurgery is one of the most responsible tasks for the modern psychiatrist. It is obvious that the selection of cases must lie in the hands of experienced psychiatrists, and it is a new challenge to our field to revive objective means of diagnosis, to adhere to a well-established terminology, and, thus, to arrive at a diagnostic grouping which resembles as much as possible the diagnostic methods in other fields of medicine.

When we postulate that schizophrenics should be given an ample trial with all types of shock treatments prior to surgery, the question arises: What is adequate shock treatment, and when should it be given up and lobotomy considered? There is still considerable disagreement on this point. As in all problems concerning schizophrenia generalizations must be avoided in view of the great variability of the disease. For reasons of orientation the various groups of schizophrenia have to be considered separately, but even breaking up the entity in the usual subtypes is not totally satisfactory. There is a great need for individual case reports rather than large statistics. Statistics are necessary as a rough means of orientation but they have many pitfalls, and additional knowledge could be obtained by publication of detailed treatment histories of as many well-documented individual cases as possible.

The requirements for adequacy in shock therapy prior to surgery differ. In acute schizophrenics I am inclined to start all patients on 20 ECT with a 3-treatments-a-week routine. If the response is striking, but the patient relapses after discontinuation of treatment, another series of 10 treatments is added. If the patient is again symptom-free, but relapses, a last attempt with ECT can be made applying the so-called intense or 'confusional' treatment: Such application of two to four convulsions every day brings the patient to a state of utter confusion and temporary organic 'dementia'. The superiority of this procedure over the three-treatments-a-week routine was not proven in our experience, but patients, even if they relapse, seem to hold the improvement longer, and a very few patients who relapsed before, stayed well after such confusional treatment.

After the failure with ECT some workers turn to electronarcosis treatment. In my own two years' experience with this method I did not see any clinical superiority of this cumbersome and unpleasant procedure over straight ECT.

When the failure of straight ECT has become obvious, insulin coma treatment is instituted without further delay. Many workers prefer to start with insulin or combined insulin-convulsive therapy without previous ECT. In patients who were treated with insulin in the first place and failed to improve, ECT should always be added before surgery is considered. One of the reasons for this is that in deciding on the adequacy of shock treatment, the adequacy of insulin treatment cannot be easily established. Only deep comas can be counted. A series of 60 to 80 deep hypoglycemic comas, not counting the light hypoglycemic reactions, constitute an adequate course of insulin treatment, but in reviewing a case, reports on insulin treatment given elsewhere are meaningless without specification on how the treatment was conducted.

In cases of full remission under any type of shock therapy but later relapse, another course, preferably combined insulin-convulsive treatment, should be instituted under any circumstances before a lobotomy is considered. In view of the undeniable side-effects as well as immediate operative risks, the psychiatrist should be reluctant to recommend surgery in cases relapsed only after a long and satisfactory remission. However, his attitude should be less conservative when a patient relapsed repeatedly, and periods of remissions were short. Where symptomatic or maintenance ECT is accepted by the patient, keeping him socially and professionally well adjusted, it should have preference before surgery. However, when remissions obtained with shock therapy are not only short but also poor in quality, early psychosurgery is justified even if only one year of continuous illness has elapsed. No strict rules should be postulated for the waiting period before surgery is considered. Each case has to be judged on its own merits. We are against waiting too long, but on the other hand, we cannot accept as legitimate reason for early surgery such factors as the presence of assumed physical contra-indications against ECT. If hypertension, cardiac disease or other pre-existing diseases are occasionally mentioned in this connexion, it must be stated that large experience with ECT has shown that there are practically no contra-indications for ECT; also fractures from previous ECT or even refusal of the patient

to accept ECT voluntarily have been reasons for early psychosurgery which we cannot accept.

There is also no evidence that previous shock treatments add to the hazards of surgery. No relation between convulsive therapy and post-operative convulsions can be assumed because convulsive therapy does not predispose to epilepsy and is even used in its treatment. If the observation of scarring of the cerebral cortex made during operations on schizophrenics is confirmed, there is at least no evidence in the neuropathology of shock treatments which permits us to connect such observations with the shock treatments, or to look upon them as a reason against their intensive pre-operative use. In schizophrenia the patients who do not respond to shock therapy remain the only candidates for psychosurgery.

Which are the schizophrenics not responding to shock therapy? There are three different groups of failures; schizophrenics who fail, although they belong to those subgroups which usually respond well to shock treatment; those in groups which are known to be poor prospects for any treatment; and those in whom shock treatment is even hardly indicated. Failures in the so-called favorable groups should be submitted to surgical procedures rather early before true deterioration sets in. This applies mainly to catatonic excitements if they fail to show their usually good response to shock therapy, and acute paranoids. Catatonic stupors are mostly considered favourable cases, but this applies rather to the symptomatic removal of catatonic symptoms than to the chances for lasting remissions which, in catatonic stupors, are much rarer than generally thought. Early psychosurgery in this group will be more cautiously recommended because results of standard lobotomies in catatonic stupors are not convincing. Some attempts were made to modify the operation in catatonic stupors, and it is my hope that the discussion will bring us some information on the experience of the British workers.

The second group of shock failures, concerns those who were poor prospects to begin with, hebephrenics. They undoubtedly remain the most primarily malignant type of schizophrenics in spite of all the new treatments. Although one sees occasional exceptions, the majority of hebephrenics with their insidious onset and course of the disease remain almost untouched by shock therapy, yet, psychosurgery will be rarely recommended in this group, because they offer few of those symptoms which respond to lobotomy or other brain surgery. If their clinical level can be at least temporarily improved by an occasional symptomatic ECT, this is preferable to surgery which may add further damage to the deteriorating effect of the disease.

The picture is brighter in the third group of shock failures, where this treatment has never more than a temporary effect. Here, several different groups can be listed in which psychosurgery is from the start superior to shock therapy, and where it will have an increasing importance if we learn better how to avoid the side-effects of the operation. Into this group belong schizophrenics in the younger age bracket with predominantly neurotic symptomatology. They are often wrongly diagnosed as neurotics, but closer psychiatric observation will reveal somatic delusions, bizarre expression of symptoms or occasional hallucinatory experiences. This group, delineated by Hoch as pseudoneurotic schizophrenia, is usually quite resistant to psychotherapy, although some of these patients can be kept on a satisfactory level of adjustment. Whenever adjustment becomes impossible and the patient's suffering unbearable, one of the various procedures of frontal lobe surgery should be seriously considered. Preceding attempts with shock therapy, usually made in view of our own fear of a damaging operation, only serve to prove that these cases respond as poorly to shock therapy as they respond well to psychosurgery. Since among this group there are often gifted people, potentially able to perform well in even highly qualified professions, it is preferable to perform partial lobotomies or any of the newer psycho-

surgical methods which have in common that they interrupt a smaller number of frontal pathways than the standard lobotomy.

Another group with poor response to shock therapy but very gratifying results under psychosurgery are cases of late schizophrenia with a predominantly paranoid symptomatology and well-preserved personality. They are often dealt with as involutional paranoids and also classified under the heading of paraphrenia. Like many patients with well-preserved personality they show no lasting response to shock therapy. They may forget their abnormal thought contents during the confusional state caused by the treatment, but their delusions return almost invariably. There is little reason to insist on long courses of shock therapy in these cases.

The psychiatrist watching the same schizophrenic under the effect of both treatment procedures sees striking differences. More detailed case reports would be helpful in this respect. So far, emphasis has been placed largely on the final outcome of the treatments, and little attention paid to phenomenological aspects. It is surprising that opinions differ in even such seemingly simple questions as to whether or not lobotomies remove hallucinations at once or only after many months or years, if at all. In schizophrenics successfully treated with shock therapy, such secondary symptoms as delusions and hallucinations disappear. Patients who fail under the treatment lose these symptoms only as long as the organic blurring of the treatment lasts. Five to ten days after the series of convulsive treatment is over, the original symptoms in the unsuccessfully treated patient return. An analogous phenomenon occurs in lobotomies, where during the first stage of organic confusion delusions and hallucinations invariably disappear. This acute organic picture continues for a longer period of time than in shock therapy, but as soon as the patient was oriented again, delusions and hallucinations reappeared in most of our cases including successfully operated patients, in whom the hallucinations had lost all their malignant influence on the patient's emotional life. It is only after another period of months or years that they seem to disappear for good. Such observation may have some relation to the old experience that in chronic schizophrenics of ten, twenty, or more years' duration the hallucinations with increasing deterioration often disappear after they have become less and less important to the patient. It may be similar in frontal lobe surgery that the psychotic experiences become colorless when the anxiety giving them momentum is removed, and finally disappear altogether. If such observations in lobotomized patients are confirmed they are quite different from shock experiences. With insulin treatment hallucinations disappear slowly because no pronounced organic blurring covers them up. With convulsive treatment they disappear more suddenly after three or six treatments. In both shock methods, if treatment was successful, they do not reappear, and it is permissible to conclude that the treatment has touched a part of the central nervous system, where, by some unknown pathophysiological mechanism, these symptoms originated. We know which structures are reached by the surgical procedures; we do not know where the shock treatments act, but thinking in organic terms we may conclude that they interfere with deeper paths of the brain than lobotomy does, and that, in favorable cases, they represent a more direct attack on the centers involved in the schizophrenic disease process.

Turning now to the group of psychoneurotics the pattern of lobotomy results is very similar to the one seen in schizophrenia, but their response to ECT differs strongly. All that can be achieved with shock therapy in psychoneurotics, with the exception of neurotic depressions, is a temporary blurring of certain symptoms.

Contrary to this, psychoneurotics treated with frontal lobe surgery may perpetuate symptoms like obsessions or compulsions half-heartedly for a while, but the anxiety connected with them will be lastingly relieved. Therefore, shock treatments in neurotics show only temporarily what psychosurgery achieves as a lasting result.

In present statistics psychoneurotics already represent the second largest group of patients subjected to the operative procedures. The newer, less destructive operations promise to enlarge this field of application considerably in those cases where psychotherapy has failed. The shock treatments have a very small place in the treatment of psychoneuroses. Modified insulin therapy is of some value in more acute neurotic conditions, but the indiscriminate use of ECT in all types of neurotics should be strongly discouraged.

The affective disorders, second group of the functional psychoses, should not be too frequently subject to frontal lobe operations, because their response to ECT is almost a specific one. Surgery in the affective psychoses will be reserved for shock treatment failures. Sometimes such failures actually concern schizophrenics with mood swings who were erroneously diagnosed as affective psychoses. In the manic-depressive group, depressions and, with more intensive treatment, also manics respond reliably to ECT. The only drawback is that ECT does not prevent future episodes. Does psychosurgery prevent them ? Here again, more individual case reports are needed to answer this question. Some cases of episodic psychoses recently reported by Jones and McCowan showed that psychosurgery can prevent future episodes. The disappearance of periodicity after lobotomy, striking in their cases, is of great theoretical interest, and if confirmed would be an important difference between the two therapeutic approaches. It would also make psychosurgery the method of choice for those patients who constantly change from depressive to manic states. They are poor prospects for ECT which only shifts them from one phase into the other.

Involutional depressions usually occur in one single episode of considerably long duration. Even recurrent cases should again be subjected to ECT rather than to psychosurgery. Those not responding to ECT are usually mixed with paranoid and other schizophrenic features. In our own experience with involutional psychoses psychosurgery could be entirely limited to such mixed cases.

A group, mostly unresponsive to ECT, is represented by cases of hypochondriasis in the older age bracket. These patients, often wrongly diagnosed as involutional melancholia, are characterized by bizarre somatic delusions which bring them closer to the schizophrenic group than to the affective disorders. While patients with agitated depressions whom these cases might resemble, blame everything on themselves, cases of hypochondriasis are often resentful of the lack of sympathy shown by their relatives, and make life miserable for themselves and their surroundings. An attempt with ECT is justified because of the possibility of a diagnostic error. But these patients are singularly unresponsive to ECT. On the other hand, they are excellent prospects for the psychosurgical procedures. In view of their poor prognosis regarding spontaneous remissions, they should be early candidates for the operation. If various aches and pains are the outstanding symptoms such cases form an interesting link to frontal lobe surgery in patients with intractable pain.

The value of either group of treatment in a number of other psychiatric conditions can be best understood by discussing certain differences in their action. Neither of them changes general personality traits, and this explains why neither of them has a place in the treatment of such personality disorders as psychopathic personality, homosexuality, alcoholism and so on, where they have been tried. Although psychosurgery leaves the basic personality structure untouched, it may be considered in rare cases of such disorders for the purpose of alleviating severe anxiety or removing disturbed, aggressive behavior. Practical results are mostly disappointing. Asocial trends remain unchanged and may even be exhibited with less restraint, although maybe with less aggressiveness. Shock treatments may find occasional application in alcohol or drug addicts in order to remove temporarily the craving during an attempt at withdrawal, but this effect will last only for days. On the other hand psychosurgery in patients operated on for pain is able to remove lastingly the cause for the addiction.

Special problems are offered by mental defectives. Here both shock therapies and psychosurgery, have been tried. Our own experience is scanty with the exception of cases of Propf-schizophrenia. These schizophrenic episodes implanted on mental deficiency have a very good prognosis under ECT. Mental deficiency as such only offers an indication for any of the treatments discussed here, when constant disturbed behavior, irritability or depressive features are the predominant symptoms of the mentally deficient person. Here, ECT has only a temporary symptomatic effect. Lobotomy has the same symptomatic effect in a more lasting way, as recently shown by Engler, but it seems to have so many hazards including higher incidence of convulsions, higher mortality and additional deterioration that Mackay discourages its use except for special cases. Therefore, the purely symptomatic effect which, here, both treatments have in common, seems to be more safely obtained by a maintenance type of treatment with electric shock.

Before we turn to the discussion of some observations of purely theoretical interest several applications of ECT in work with psychosurgery will be described. For one, ECT is an extremely useful test to determine the prognosis in certain cases under consideration for surgery. This 'Prognostic Electric Shock Test' helps to differentiate between reversible and irreversible symptoms. It may be difficult to decide whether an uncommunicative chronic schizophrenic is empty or just blocked. Only if three or four ECT show that he was merely blocked, can anything be expected from psychosurgery or, for that matter, from any therapy. Many other psychotic symptoms can be likewise washed away temporarily by three or four ECT. The positive outcome of this test, though, should not yet be taken as a guarantee for a favorable outcome of the operation, since many other factors of his illness as well as his prepsychotic personality figure as prognostically important. An entirely negative response to the prognostic ECT test, however, seems to be of ominous prognostic significance.

Another application of ECT in direct connexion with the operation is its use as an anesthetic during transorbital lobotomy. On Dr Freeman's suggestion we have applied it routinely with this procedure. The effect of these ECTs must be taken into consideration when judging the early result of a transorbital lobotomy which is often deceivingly good for a week or ten days, thus corresponding to the duration of the transient ECT improvement.

Another application of ECT in work with psychosurgery is its use after lobotomy. Some authors claim occasional good results in patients who have failed under shock treatment prior to the lobotomy. We were not able to confirm this, maybe because our own patients probably had a particularly large number of shock treatments before they were turned over to the brain surgeon. This raises the question whether a number of patients appearing in statistics on lobotomy might have improved under further shock treatment if such had been given. There is no objection against ECT after lobotomy, but there is no proof yet that such a combination will increase the number of cases with favorable outcome.

It was tempting to investigate how far certain differences between shock therapy and psychosurgery may contribute to our understanding of their mode of action. While in the field of shock treatments the actual gain in theoretical knowledge was greatly disappointing, much new information was obtained by work with the psychosurgical methods. The hope to gather more information from a comparison of the two groups of treatment encouraged the following thoughts.

An important difference is the increasing evidence that the psychosurgical methods represent a quantitative approach, while the shock methods come nearer to a qualitative one. Shock therapy in those psychiatric disorders, where they are mainly effective, suggests a direct therapeutic approach on the site of the illness. No such direct approach can be seen in lobotomies. There is no area in the frontal lobes which can be considered as being responsible for basic symptoms of the psychiatric con-

dition for which the operation is applied. Recent evidence against specific function of different areas is the work by Scoville, who showed that undercutting of three different frontal lobe areas yielded the same clinical therapeutic results. My own impression from the psychiatric evaluation of cases operated in different ways strongly indicates that the effect of the various procedures depends entirely on the number of frontal lobe fibres cut. The original technique of transorbital lobotomy severing only a fraction of fibres cut in the standard prefrontal lobotomy had very little effect but yielded slightly better results when repeated in the same patient. Thereby we assume that the cuts made are never identical, and that with the second intervention additional pathways are cut. Also, transorbital lobotomies with the additional deep frontal cut are said to be more effective. Unilateral lobotomies are effective in some cases but inadequate in most psychotics. Topectomies and gyrectomies produce fewer side-effects because they represent a less extensive interception of cortico-thalamic pathways and, therefore, are less intensive operations regarding both therapeutic effect and side-effects. The most effective but also most destructive operation is still the standard lobotomy. Here again, our material contains a number of cases where, under direct vision, smaller cuts were made in order to avoid side-effects, and the results turned out to be inadequate, while re-operating with broader destruction of pathways led to the desired clinical effect. The same is demonstrated by cases in whom an anterior frontal cut was ineffective, while a later, more posteriorly located cut proved to be effective; since a posterior cut severs a far greater number of frontal lobe fibres than a cut nearer to the frontal pole, this is again in favour of a quantitative explanation of the effect of frontal lobe surgery. It must be our goal to find the right amount of surgery for the individual psychiatric case.

An entirely different picture presents itself in the shock treatments. In ECT the maximum effect is visible though maybe only temporarily, after an average of four convulsions, when in favourable cases such as depressions, the entire psychotic syndrome disappears. At this time, clinical and electro-encephalographic evidence of brain damage is still negligible. The improvement is usually not even a gradual one, but a patient who is unchanged up to the third treatment, may suddenly clear up completely after the fourth treatment. A quantitative factor in shock treatments can be seen only in the fact that the number of repetitions of the therapeutic convulsion, in certain disorders such as schizophrenia, improves the lastingness of the result. In insulin therapy the effect is more gradual, but the optimum result is also obtained relatively early in favorable cases, and here too repetition of the comas contributes chiefly to a more permanent result.

The question of relapses after shock therapy and psychosurgery reveals other differences. Fully aware of the danger of generalizations, we still feel justified in drawing certain conclusions from our own material and from the experience of others. It is undeniable that the worst drawback in all shock treatments is the tendency to relapse. The relapse rate is unduly high when we include those cases who relapse during the first few weeks, and who should rather be listed as failures. However, even in adequately and successfully treated cases the rate of late relapses is still considerable. On the other hand, true relapses after lobotomy seem to be rare. A lobotomized patient who has reached a certain equilibrium, even if he shows only a fair result, will not easily relapse into the same psychotic syndrome he had offered prior to the operation. We usually saw this only in patients in whom partial operations had been performed. A particularly striking relapse occurred in our lobotomy material after a spectacular improvement which, significantly enough, was not even accompanied by the usual personality changes. This patient went again into a full-blown catatonic excitement with all the features shown previously. Re-operated with a larger cut she showed a result which could not be called more than fair, but this time, was permanent. Reports on thalamotomy also mention true relapses

only in cases where the lesion was too small. In extensive psychosurgical operations relapses do not seem to occur if we list as failures rather than relapses those where the symptoms never disappeared except for the time of the immediate post-operative organic reaction. We cannot consider as relapses those patients who, in spite of the operation, deteriorate further; it does not surprise that the disease progresses and particularly those primary schizophrenic symptoms which are known not to be influenced by frontal lobe surgery. If those differences which we tried to work out are confirmed by future experience they seem to suggest that shock therapy represents an entirely different and more direct approach to the site of the sickness. Thinking in anatomical terms this site must be in some part of the brain other than the frontal lobe or thalamus because in surgery, the site of approach is known to be limited to these parts.

Study of the organic symptoms after lobotomy has contributed much to our knowledge. Therefore, a comparison between the organic reactions of lobotomized and of shock-treated patients would be in order. The lobotomized patient shows an initial organic reaction close to dementia. When he becomes more responsive, he offers a Korsakoff-like syndrome which is characterized by a strange spottiness of recent and remote memory loss until he emerges from these temporary pictures and shows a more permanent syndrome which has some frontal lobe characteristics but in which he also behaves much like any brain-injured person. He is less differentiated and functions in many ways differently than before. He is oversensitive to noises and other crude sensory stimuli, but less sensitive to more differentiated ones. The shock patient has none of these permanent characteristics of a brain-injured person. During the series of treatments he may go through various stages into a similar organic dementia, as the lobotomized patient but ends up without any organic traces. In insulin therapy even the temporary organic symptoms are rather negligible. Therefore, it can be concluded that permanent organic psychiatric symptoms are not necessary for the recovery of psychotics. There is evidence that also the initial but transient organic syndromes seen in ECT as well as in lobotomy are unimportant for the therapeutic effect. In both treatments a correlation between the depth of the confusion and the final outcome has been claimed but in neither of them was this borne out by our personal experience.

Finally, some psychological differences of the various methods regarding the patient's post-treatment amnesia for his symptoms should be mentioned. The insulin patient often has good insight and remembers most of his pathological experiences. The ECT patient remembers little of his sickness, and it is only after weeks or months that he remembers some of his symptoms. The lobotomized patient, if he loses his symptoms, has hardly any insight. He even has a strange way of denying any improvement. While the shock patient realizes the difference and is usually very grateful, the lobotomized patient never is. This does not seem to be a simple lack of gratitude but rather the inability to remember his symptoms. There is no explanation available for this fact which makes lobotomized patients so different from shock-treated ones. These and other psychological differences should be studied because of their possible importance for the localization of certain psychological reactions in the brain. To give a few differences: confused shock cases, even when deeply confused, are never as stubborn as lobotomized patients when their mistakes are corrected. Also their answers are never so amazingly wrong and yet presented with such certainty as in lobotomized patients. Furthermore, the rules of retrograde amnesia and subsequent return of material in chronological order which is surprisingly constant in ECT, is never displayed as clearly after lobotomy, where for some time after the operation, the patient offers a strange mixture of recent and remote memory loss. Another observation which invites some meditation is that in patients, who during a transorbital lobotomy receive three or four ECT as a means of anesthesia, the sen-

sorium becomes clear apparently faster than when a patient had three or four electric shocks without a lobotomy.

Of the many basic questions brought up by the new methods one may be briefly mentioned. Does man lose the ability to react with functional psychoses when we diminish his brain tissue? We have no proof that animals with less brain tissue have functional psychoses. Since they can be relieved in man by diminution of functioning brain tissue, it is possible that this is the way how psycho-surgery acts. The absence of true relapses after large operations would support such assumption. Shock treatment does not destroy brain tissue and certainly does not reliably prevent psychosis.

It is not my intention to lose myself in speculations, but I wanted to show how many avenues of thought are opened up by the new therapeutic approaches. We probably have to formulate certain hypotheses if we want to find newer and more effective treatments to which the two ways of approach to the treatment of mental illness compared in this paper may lead us some future day. We know something of the mode of action of psychosurgery but nothing about the way shock treatments work. Both treatment procedures leave many basic questions still open, and this is not surprising as long as the diseases we are treating are not understood. However, it is a fascinating thought that our therapeutic attacks on these disorders might answer some questions regarding their actual pathology.

Before closing I wish to admit that the title of this paper, namely 'Relations of lobotomy to the shock treatments', had a more negative than positive meaning, Yet, it was hoped that by working out their differences, not only their respective indications could be specified, but that our attention would also be focused on some points of theoretical interest which future research may clarify.

Discussion

Dr E. Cunningham Dax said that this was a difficult subject which had been admirably dealt with by Dr Kalinowsky from his very great personal experience.

In opening the discussion one might draw similarities between the shock therapies and leucotomy in so far as they were both non-specific physical methods of treatment, which had not thrown the expected light upon the nature of mental illness, although they had done something towards furthering classification. He noticed that Dr Kalinowsky said that they must adhere to a well-established terminology but one of the advantages to emerge from the various treatments, now investigated for some years, was that terminology might be altered as a result of what had been found.

It was interesting to notice that both leucotomy and the shock treatments had undergone modification ; in convulsion therapy the method had largely changed from drugs to electrically induced convulsions and later to the elimination of the convulsions, whilst the incisions for leucotomy had moved from section of the greater part of the white matter of the frontal lobes to selective incisions, cortical undercutting, topectomy, and thalamotomy. In the earlier stages of the work on convulsion therapy it was considered that the convulsion itself must produce the effect as subconvulsive applications were of no value. It would also be remembered that Gillespie suggested that the sub-convulsive state produced by prolonged narcosis was responsible for its success and it had also been said that the early convulsions of insulin coma therapy were like the continued insulin and convulsive therapies – responsible for better results in treatment. The work on curare and the anti-convulsant drugs had raised doubts about these points, and by comparison it was of interest that the early lesions made in leucotomy operations embraced the upper and middle portions of the frontal lobes and not infrequently caused epilepsy, whilst the later lower incisions had produced comparable results in series of cases practically free from epileptic fits.

This suggested some common heading, but he was rather worried by the way in which Dr Kalinowsky had assumed (or so it seemed to him) from the beginning, that

these various forms of therapy were complementary. It would have seemed that shock therapy was a necessary preliminary to almost any other form of treatment, but one wondered whether in certain cases shock therapy might actually have an adverse effect.

It has been suggested that the effects of convulsion therapy are due to an electrical leucotomy, even if reversible. This mainly rests on animal experiments where comparatively large amounts of electricity were used; he had, however, seen a spider-like haemorrhage on the surface of the brain in a case opened up for a leucotomy operation directly following an electrically induced convulsion.

It would seem that a means of investigating the relationship between the shock therapies and leucotomy might be to take some cases successfully treated with leucotomy and a comparable number who had failed to react and to see if any difference had been shown in the reactions of the two groups to the various shock therapies before operation. He had taken a series of 50 consecutive cases discharged after operation and compared them with 50 consecutive cases unsuccessfully treated by this means, the two series dating immediately prior to last March. There are obviously many criticisms which may be made of this somewhat crude comparison and it could not be expected to do more than point towards any further investigations which could be made in a general way. In fact, analysis of the table shows that the results are not statistically significant.

	Reaction of patients to shock treatments prior to:			
	A. Successful leucotomy		*B. Unsuccessful leucotomy*	
	Improved	*Not improved*	*Improved*	*Not improved*
Prolonged narcosis ..	6	4	5	3
Insulin comas	9	6	10	6
Cardiazol	4	6	2	9
ECT	32	20	31	30
Electro-narcosis	—	4	—	2

Dr Kalinowsky had already shown that preliminary-ECT was useful as an aid to prognosis in patients before leucotomy. The speaker's own figures were small, but they did not confirm that observation. Further work was obviously necessary.

The matter of personality changes loomed large in the discussion of leucotomy, but he believed that the greatest advantage of the operation was that it could influence personality whereas the other shock therapies had no comparable effect. Personality change did not necessarily mean deterioration; one did not see what one might call 'the microscopical' effects of the operation by selective incisions, but 'the microscopical' results could be demonstrated by some tests. It might be that the maximum number of fibres could be divided with the smallest incisions when they were made in the lower quadrants, but at least many association fibres were spared, the extent of the damage was less and fibres from the orbital cortex were divided. The feeling of the neurosurgeons that 'it does not matter what we cut' to produce an effect was emphasizing the quantitative rather than qualitative aspect. He felt that the psychiatrists should rally their forces and say that the complicated structure of the brain with its very intricate fibre connexions, had not been devised by accident and in spite of all that they had been told he did not believe that the same effects were obtained from a section of one part of the frontal lobe as another part. His work and experiences did not confirm that.

The shock therapies and leucotomy had one great point in common which was that they provided a magnificent stimulus to psychiatric treatment and research. They had turned the pages of several new books and thousands of papers in the work on psychological medicine.

Dr E. B. STRAUSS (London) said he had very much appreciated Dr Kalinowsky's admirable clinical presentation of his subject. From his lesser experience he could confirm most of what he had said. There was just one point he would like to start off with. He was emboldened, in spite of the presence of Professor Freeman, to hope that a term used by Dr Kalinowsky, namely 'frontal lobe surgery', might replace 'psychosurgery', to which there were many objections.

With regard to the effectiveness of electronarcosis which Dr Kalinowsky mentioned more or less *en passant*, he thought that the time was not yet ripe to assess its clinical value. He had worked on this method and was now employing a different type of current from what was habitually used in U.S.A.: and his first impressions were that in the group of psychiatric disorders which he had come to call obsessional psychosis, electronarcosis had something to offer in the way of permanent improvement. There was a group of early paranoid schizophrenic patients who seemed to respond to pulse-wave electrocoma even better than to insulin shock therapy. There was, perhaps, one small point on which he might offer a word of caution. Dr Kalinowsky stated that there was no indication against the application of electrical convulsion therapy to leucotomized patients, but he was not sure that that was true. There were certain indications, he thought, that the scar-tissue which formed after leucotomy acted as an abnormal conductor of the electric current. He thought it was significant that in the few fatal cases following electrocoma and ECT a significant number had occurred in leucotomized patients.

Dr TURNER MCLARDY said that there were two small points in Dr Kalinowsky's general conclusions which he would like to query. The first of these was that relapse to the *status quo* was never complete after a full cut. From a review of all the available literature and considerable personal material, he and Davies (*J. Neurol. Neurosurg. Psychiat.*, 1949, **12**, 231) had come to the conclusion that many of the symptoms and syndromes characteristic of the functional psychoses could recur in full after practically complete bilateral isolation of the whole prefrontal cortex from its long fibre connexions. Perhaps the most convincing evidence was that of Peyton, Noran and Miller (*Amer. J. Psychiat.*, 1948, **104**, 513) who had performed lobectomy operations on psychotics, entailing the almost complete bilateral removal of the prefrontal regions. In a private communication they had said that of the original 14 cases 2 had shown a relapse: one, a chronic catatonic schizophrenic who had improved appreciably, started to regress one year after operation into a state of severely deteriorated hebephrenia; the second, a chronic puerperal psychotic who had shown marked improvement, regressed almost completely to her pre-operative state three months after the operation.

The second point concerned Dr Kalinowsky's impression that there seemed to be no increased response to convulsion therapy after leucotomy. His own general impression, derived from the literature and personal material as outlined in the article already quoted, was that there is a tendency towards increased response to environmental influences, including electrical convulsion therapy and insulin therapy.

Finally, perhaps it would be relevant to mention that at the Maudsley Department of Neuropathology 18 brains had been examined in detail from patients submitted to electro-convulsion therapy from 15 to 150 times, and in none of them was there any histological evidence of pathological change in any part of the brain or brain stem.

Dr A. SPENCER PATERSON (London) thanked Dr Kalinowsky for his excellent paper, but he pointed out that in this country many psychiatrists had found electronarcosis a very useful method of treatment. He had found that the technique of giving 'intensive ECT', i.e. shocks in quick succession, had often effected a recovery, when ordinary

ECT had failed. The results with electronarcosis were even better than with intensive ECT and yet the unpleasant side-effects of the latter were avoided. In England it had not been found necessary to give the high currents favoured elsewhere. In the first half-minute about 200-240 m/A were given instead of 400 often used in the U.S.A. or 600 in Italy.

When simple ECT failed in depressions, some psychiatrists were apt to recommend a leucotomy, but his co-workers had found that electronarcosis often succeeded in these cases, especially with patients in middle life, even if there were hallucinations, delusions or severe obsessional symptoms.

The expression 'electrocerebral treatment' was a convenient one to include electroshock or electronarcosis (ELN). Three years previously when ELN was started, there were still many psychiatrists who disliked ECT and who used it as little as possible. The speaker, however, had considered that the best course was to make a careful study of various techniques in order to produce the maximum therapeutic effect with the minimum of noxious side-effects. As the result of three years' work it could safely be said that it was not the actual fit which caused the therapeutic effect. It was a mistake to think that ECT was the last word in electrocerebral treatment. There was already evidence that with correct size of electrodes and correct placement, and with a particular type of wave a therapeutic coma could be produced without causing a fit or even a rise of blood pressure. He said in conclusion that electronarcosis as used at present had a definite place in psychiatry and that with further work still better results might be obtained.

Dr KALINOWSKY, in reply, said that he thought the discussers had treated him very well considering the many controversial points which he had brought forward. There were a few points on which he could answer Dr Cunningham Dax. It was disappointing that the hopes to learn something about specific function in special areas of the frontal lobe had not been fulfilled. His great interest in psychiatry would always be to find localization of psychiatric syndromes, but two facts emerge from the experience with psychosurgery which is much larger than any previous experience based on brain tumour or other neurological diseases. Psychotic syndromes as seen in the major psychoses do not originate in the frontal lobe; and there is no specificity of function in special areas of the frontal cortex.

Dr Strauss had interested him very much when he said that he obtained better results with electronarcosis than had been obtained in America. It is very difficult to compare shock treatments. They were given one after the other, and there is always a summation of effect. He always pointed out to those who gave one treatment inadequately and then considered the next type of treatment as being better, that inadequately treated patients are unsuitable evidence that the next treatment was better. Furthermore, if one gave electronarcosis in certain types of patients before carrying out any other type of treatment the question was how the patient would have responded to the usual electroconvulsive treatment. Nobody had yet made a really comparative study of the effect of the various treatments adequately applied, and his own feeling was that all the treatments had very much the same results, although most people did not agree with this point. It was interesting for him to hear of patients in whom post-operative electric shock was effective. There was no reason why it should not be. It was possible that sometimes organic symptoms were removed which came out after the operation because all types of organic psychotic reactions could be influenced by electric shock, and there was no reason to think that it would not be possible with post-leucotomy reactions as well. He did think, however, that those who felt that it was absolutely necessary to give post-operative electric shock in a large number of cases, actually removed symptoms which

could have been removed prior to the operation if shock treatment had been applied adequately.

He was interested in what Dr McLardy said about the relapse rate. Future experience would show if his own generalization referring only to patients with extensive operations, was wrong. He thought when a patient who had had lobotomy further deteriorated after some time that this was something different from a relapse. In many patients most symptoms of schizophrenia were not removed by lobotomy in the first place, and there was no reason why the disease as such should not progress and why the patients could not deteriorate further even if the lobotomy had improved or modified one set of their symptoms but had left what might be called the primary symptoms of schizophrenia.

He wished to say once more that the individual cases with detailed reports on all types of treatment given and their effects on the patient should be published much more frequently rather than mere statistics on large groups. It was disappointing to see almost identical improvement figures in all types of treatments. One had to learn which treatment is effective in which individual case; this one can only learn from detailed treatment histories of individual cases.

The question of daily confusional electric shock treatment was difficult to decide, but those who were in favour of confusional treatment were also those who gave many treatments and he was not surprised that they had results in patients where previous routine treatment was ineffective. It was difficult to prove whether confusional treatment would have done more had it been carried out with the same number of treatments given at longer intervals and less organic confusion.

The question of different currents was interesting. He could not be convinced so far that any of the treatments with different types of current were superior to others, and he was always a little sceptical about the whole approach because it was not the electrical current which caused the therapeutic improvement but it was the convulsion or the coma. Application of electricity without convulsions had been tried before the shock treatment era, and there had been no improvement in the psychoses.

The main conclusion to be drawn from the discussion on all these treatments was that there was an active approach to disorders which up to about fifteen years ago, could not be attacked to any extent. It would be through their differences of opinion that psychiatrists would make progress and get more patients out of their mental suffering.

THE PHYSIOLOGICAL BASIS OF SHOCK THERAPY[1]

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The thesis presented today is in essence the same which was published in 1938 [1] but its factual basis has been widened considerably. Its starting point was the clinical observation that functional mental diseases and particularly schizophrenia involve autonomic disturbances probably at the diencephalic level. Tests in which the reactivity of autonomic centers under conditions of stress was studied on controls and on schizophrenics seem to show that the responsiveness of sympathetic centers is diminished in the latter group. That the chief difference concerns higher autonomic centers is indicated by the fact that certain autonomic reactions proceed within normal limits in schizophrenics whereas emotional stress acting at the hypothalamic level reveals a diminished sympathetic reactivity. Experimental analysis of the procedures

[1]Supported in part by a grant from the Office of Naval Research.

used in the shock therapy of mental diseases shows that each one produces a powerful stimulation of sympathetic centers although the physiological mechanism leading to this stimulation is fundamentally different in procedures such as insulin hypoglycemia and electroshock. Finally, observations on patients before and after shock treatment suggest an increase in sympathetic central reactivity with clinical improvement.

Let us grant for a moment the triad of observations on the relation between autonomic reactions and schizophrenia, i.e. diminished sympathetic reactivity of schizophrenics, prolonged excitation of sympathetic centers in shock therapy and, finally, increased sympathetic responsiveness with increasing clinical improvement. Furthermore, let us infer that these data strongly suggest that the sympathetic system plays an important role in the pathogenesis and therapy of mental diseases. Even then our problem, to arrive at a physiological analysis of these relations, is by no means solved.

To complete the picture it is necessary to take into consideration the fact that the diencephalon contains not only an efferent system through which autonomic and somatic effects are induced (Cannon's 'downward discharge') but also an afferent system through which the hypothalamus is linked with the cortex. Experiments indicate that hypothalamic excitation causes both upward and downward discharges and lend support to the assumption that even without overt stimulation tonic impulses influence visceral as well as cortical activity. These hypothalamic-cortical impulses are not sympathetic since they persist after cervical sympathectomy or high spinal transsection but they form an integral part of hypothalamic activity. Since under various experimental conditions a distinct parallelism between the autonomic 'downward discharge' and the hypothalamic-cortical 'upward discharge' could be seen it is understandable, at least in principle, that excitation of autonomic hypothalamic centers may alter cortical activity and thereby behavior through action on the cerebral cortex. Experiments which showed significant changes in conditioned reactions as the result of 'shock therapy' in normal animals may therefore be interpreted as a physiological demonstration of this action.

Before presenting some of the data upon which this interpretation of the mechanism of shock therapy is based one criticism should be disposed of. Several authors [2, 3] noted that the injection of adrenaline was without benefit in schizophrenia and felt that this observation disproved the validity of the hypothesis just presented. This seems to be, to express the matter charitably, a rather naïve reasoning. The emphasis in previous publications from this laboratory has been on the excitation of autonomic centers at a high (probably diencephalic) level, the long persistence of these effects and the consequent alteration of cortical activity due to changes in hypothalamic-cortical relations. That stimulation of autonomic centers such as the hypothalamus is accompanied by the secretion of adrenaline is undoubtedly true; however, the assumption that the secretion of adrenaline represents the sole important effect is logically and physiologically erroneous since the complex action of central autonomic excitation is arbitrarily identified with only one of the factors involved. Consequently, from the point of view of the theory under discussion a beneficial action from the injection of adrenaline was not expected. As a matter of fact it was shown earlier in collaboration with Darrow [4, 5] that adrenaline actually diminishes hypothalamic sympathetic excitability. Although the secretion of adrenaline may be taken as an indicator of central autonomic discharges numerous central effects are obviously present even after removal or denervation of the adrenal medullae. It is therefore not surprising that behavior changes could be induced through various forms of so-called shock therapy not only in normal but also in adreno-demedullated animals.

These experiments again support, at least for the physiological experiment, the assumption that procedures used in shock therapy act primarily through central autonomic discharges and through their effect on the cerebral cortex.

It is now my task to present the chief evidence for this theory although time does not permit a complete discussion of the literature.[1] Diminished responsiveness of the sympathetico-adrenal system in schizophrenics has been observed by numerous authors. Finkelman [6] states that exposure to cold results in a greater fall in temperature and a lesser rise in oxygen consumption in schizophrenics than in normals. Both effects are accounted for by deficient secretion of adrenocortical hormones since adrenalectomized animals show a greater fall in the temperature of the body and a lesser rise in oxygen consumption than unoperated animals (Horvath, Hitchcock and Hartman [7]). However, this alteration in the function of the adrenal cortex has to be considered in the light of work in which a relation between cold and adrenal medulla was thoroughly established. Hartman, McCordock and Loder [8] demonstrated the excitation of the sympathetic adrenal system in cold, and recent experiments showed that the activity of the adrenal cortex on exposure to cold is regulated, at least in part, by the degree of adrenomedullary secretion (Gellhorn and Frank [9]). In view of these findings it is suggested that the lessened reactivity of schizophrenics to cold is due to the fact that the secretion of adrenaline from the adrenal medulla initiated by the cold stimulus is diminished in these patients and that consequently the adrenocortical reactions are likewise deficient.

The failure of the blood sugar to rise in conditions of apparent emotional excitement (Whitehorn [10], Gellhorn, Allen and Feldman [11], Parsons and collaborators [12]) seems likewise to indicate a diminished responsiveness of the sympathetico-adrenal system and the diminished vasomotor pressor response and lessened reactivity of the psychogalvanic reflex [13], which is based on a cortical sympathetic reflex on the sweat glands, requires a similar interpretation.

These data would suggest a subnormal reactivity of the sympathetic centers in the hypothalamus in functional psychoses. Since many conditions such as anoxia, cold and emotional excitement which previously were shown to induce a sympathetico-adrenal discharge (Cannon [14]) call forth at the same time a vago-insulin discharge (Gellhorn and collaborators [15]), it may be expected that an imbalance in the autonomic centers could be demonstrated in schizophrenia. Such interpretation is supported by experiments in which blood from excited psychotic patients and from normal individuals (medical students subjected to a three-hour examination in physiology) was tested on hypophysectomized-adrenodemedullated rats. These animals react normally to adrenaline and are highly sensitive to insulin [16]. A predominance of the sympathetico-adrenal effect would appear as a rise in blood sugar in a test animal while a prevalence of the vago-insulin discharge would result in hypoglycemia. The results showed that in practically all psychotics the balance of the autonomic centers was shifted to the side of the vago-insulin system since marked hypoglycemia appeared in the test animals [11]. However, in the control cases the blood sugar of the test rats was either increased or unchanged. In view of the fact that in experimental animals the responsiveness of the sympathetico-adrenal system may be altered by several physiological factors [17, 21] while no such changes could be induced in the reactivity of the vago-insulin system, the data would suggest that the imbalance was due to a diminished reactivity of the centers regulating the activity of the sympathetico-adrenal system and not due to an increase in the responsiveness of parasympathetic centers.

Certain clinical and experimental data seem to give further support to this interpretation. Diminished activity of the thyroid gland in at least a certain number of schizophrenics has been found by several authors (Hoskins [18], Rheingold [19]) and Gjessing [20] showed that cases of periodic catatonia were improved on treatment with thyroxin. On the other hand, it was found that the sympathetic reactivity of animals to metrazol as measured by the degree of hyperglycemia was markedly diminished

[1]Concerning the older literature cf. E. Gellhorn, *Autonomic Regulations*, New York, 1943, Chapter 19.

after thyroidectomy and increased by administration of thyroxin (Gellhorn and Feldman [21]). The latter phenomenon must be interpreted as being due to increased reactivity of the centers since on administration of subtoxic doses of thyroxin the hyperglycemic reactions to the centrally acting metrazol is increased while the hyperglycemic effect of the peripherally acting adrenaline is unchanged. It is also of interest to mention that no evidence for an action of thyroxin or thyroidectomy on the vago-insulin system was found.

The next question concerns the nature of the essential changes which occur in the central nervous system as the result of "shock" therapy. Although the speaker is not qualified to evaluate clinically the various forms of shock treatment it may be stated that apparently widely different forms of treatment such as convulsions induced either chemically or electrically, as well as hypoglycemic coma and barbiturate treatment, call forth an improvement which suggests a common causative factor. This, I believe, lies primarily in the excitation of the sympathetico-adrenal system.

That electroshock or metrazol causes a sympathetico-adrenal discharge is easily shown by the hyperglycemia seen in normal animals. After removal of the adrenal medullae electroshock induces a hypoglycemia while in adrenodemedullated-vagotomized rats the blood sugar remains unchanged after electroshock [22]. These experiments indicate that both vago-insulin and sympathetico-adrenal systems discharge as a result of electroshock and that in normal animals, at least as far as the blood sugar changes are concerned, the reactivity of the sympathetico-adrenal system far outweighs that of the vago-insulin system.

Recent experiments suggest that this discharge is only the starting point of a series of reactions which involve the major part of the endocrine system. It has been shown that conditions such as convulsions (Gellhorn [23]) induce a lymphopenia which is caused by increased secretion of adrenocortical hormones. Since this reaction is absent in adrenodemedullated animals it may be inferred that the secretion of adrenaline initiates alterations in the secretion of adrenocortical hormones through the mediation of the hypophyseal adrenotrophic hormone. This interpretation is supported by the observation that injection of minute quantities of adrenaline induces lymphopenia and that this reaction is absent in adrenalectomized rats [24].

The physiological changes accompanying metrazol convulsions likewise indicate excitation of the sympathetico-adrenal system. Alterations in blood sugar of normal, adrenodemedullated, and adrenodemedullated-vagotomized rats are in good agreement with those previously described for electroshock. The experiments are again an indication of a discharge of both the vago-insulin and sympathetico-adrenal systems with the latter predominating. The marked contraction of the sympathetically innervated nictitating membrane, the maximal dilatation of the normal but not of the sympathectomized pupil and the occurrence of sweating from the foot pads of the cat (galvanic reflex) give further indication of a sympathetic discharge. These sympathetic discharges persist in spite of ligation or removal of the adrenal glands. There is also evidence of parasympathetic discharges but in general, except for the initial fall in blood pressure (vagal excitation), the sympathetic effects predominate [25].

Two more procedures, the sleep treatment ('Dauerschlaf') and the insulin shock need yet to be treated. In contradistinction to previously discussed methods of shock therapy they do not involve convulsive activity. There is no need to give a complete analysis of the changes in the central nervous system which occur in barbiturate narcosis or at the various stages of insulin hypoglycemia. Suffice it to say that in both procedures cortical activity is depressed as indicated by the slowing of the potentials in the EEG in hypoglycemia and the occurrence of grouped sleeplike potentials in EEG and ECoG in barbiturate sleep. Whereas in electroshock or in

chemically induced convulsions cortical discharges are greatly increased, at least temporarily, the activity of the cortex in hypoglycemia and barbiturate sleep is diminished. Nevertheless the functional changes in the autonomic nervous system are similar in both groups.

The occurrence of a sympathetico-adrenal discharge in hypoglycemia is well established by numerous investigators [26]. Sympathectomized animals are hypersensitive to insulin [27], adrenaline appears in the blood during hypoglycemia (Tietz, Dornheggen and Goldman [28]) and the adrenaline content of the adrenal medulla is diminished (Saito [29]). That the excitation of the sympathetic system is not confined to the release of adrenaline is shown by the fact that insulin hypoglycemia causes constriction of the denervated nictitating membrane in animals in which the adrenals had been functionally eliminated. The contraction of the denervated nictitating membrane appears therefore to be due to the release of sympathin from postganglionic sympathetic nerve endings (Partington [30]). There is likewise evidence for the fact that as in experimental convulsions, hypoglycemia leads to a fall in lymphocytes which is partially initiated by a sympathetico-adrenal discharge (Gellhorn and Frank [31]).

As to the action of barbiturates on the autonomic nervous system it may be said that they raise the blood sugar temporarily [26]. This effect is due to a sympathetico-adrenal discharge since it is absent after adrenodemedullation. This interpretation is supported by the observation that barbiturates lead to a temporary dilatation of the chronically denervated pupil suggesting again a release of adrenaline (Gellhorn [32]).

Although it may be said that procedures leading to convulsions (electroshock, metrazol) as well as barbiturate sleep and insulin hypoglycemia cause an excitation of the sympathetico-adrenal system the mechanism involved in its initial stages seems to be quite different in the two groups. Whereas the former are accompanied by maximal convulsive discharges which occur in cortical as well as in subcortical structures, signs of greatly diminished cortical activity appear in the latter. In view of the fact that the inhibitory role of the cortex on somatic and autonomic functions is well established it is suggested that in barbiturate sleep and insulin hypoglycemia the sympathetico-adrenal discharge is not the result of an excitation of autonomic centers but due to their release from cortical control. On the other hand it is assumed that electrically as well as chemically induced convulsions lead to a direct excitation of subcortical autonomic centers, but, in addition, it is not unlikely that excitatory processes in the hypothalamus are favored through release from cortical dominance since in the course of convulsive activity the cortical potentials may completely disappear for some time.

The data presented thus far seem to justify the conclusion that convulsions (electroshock, metrazol) and non-convulsive procedures of shock therapy (hypoglycemic coma) as well as barbiturate sleep lead to an excitation of the sympathetico-adrenal system. That autonomic centers at the medullary and hypothalamic level are involved seems to follow from several studies although this phase of the investigation is by no means complete.

Gellhorn and Darrow [4, 5] showed that the reflex effects of sciatic stimulation on blood pressure, pupillary dilatation, contraction of the nictitating membrane and sweating are increased on administration of metrazol and that such effects of augmented sympathetic responsiveness are independent of convulsive activity and secretion of adrenaline since they are observed also in curarized animals and after adrenalectomy. Of particular interest is the observation that metrazol increases significantly the reactivity of the hypothalamus. If the contractions of the sympathetically innervated nictitating membrane are recorded under conditions of central (hypothalamic) and peripheral (preganglionic fibers of the superior cervical sympathetic)

electrical stimulation before and after injection of metrazol, it is found that this drug greatly increases the responsiveness of the nictitating membrane to central but not to peripheral stimulation. Moreover, this effect can be shown to persist for many minutes. Such a persistence of central autonomic discharges is likewise apparent from periodic contractions of the nictitating membrane which may continue after metrazol administration for a considerable time after the convulsions have ceased.

Increased reactivity of autonomic centers in hypoglycemia is inferred from a study of the pressor effects induced by inhalation of oxygen-nitrogen mixtures at various blood sugar levels. It was found in experiments on anesthetized animals [33] as well as in man [34] that the vasopressor action of anoxia increases with decreasing blood sugar level and that a similar effect can be demonstrated when carbon dioxide is used as a stimulus [35]. Since carbon dioxide continues to have an increased vasopressor action in hypoglycemia after denervation of the sino-aortic receptors it may be said that the reactivity of autonomic centers is increased to reflex stimulation (action of anoxia on the chemoreceptors of the sino-aortic area) and to direct stimulation of sympathetic centers (carbon dioxide pressor effect in the sino-aortic denervated animal). Similarly it was found that the blood pressure rise to increased intracranial pressure [36] increases with falling blood sugar and that this result persisted after sino-aortic denervation. Although it may be stated with confidence on the basis of these experiments that the reactivity of the sympathetic centers to afferent stimuli originating in the chemoreceptors of the sino-aortic region and to direct stimulation is increased in hypoglycemia it remains to be shown that these changes affect medullary as well as hypothalamic centers.

In order to link the action of various forms of 'shock therapy' on the centers of the autonomic system to the therapeutic effects seen in man, the persistence of these effects becomes a matter of major interest. Studies on rats gave evidence that the increased sympathetic reactivity resulting from repeated electroshock continued for a number of days as indicated by the greatly increased hyperglycemia following a standard test with anoxia (Gellhorn and Safford [37]). No such evidence could thus far be obtained for the action of repeated insulin comas. However, the failure of the blood sugar to rise above the control level in response to the standard stimulus was shown to be due to the fact that repeated insulin comas practically abolish the glycogenolytic effect of adrenaline. Further studies on prolonged effects of repeated insulin coma on autonomic centers are desirable with other indicators than blood sugar for the functional changes occurring in the sympathetico-adrenal system.

It is not the task of the present paper to develop a theory of the physiological foundations of behavior but it may be taken for granted that behavior in the human, at least, is determined to a large extent by the reactions of the cortex. On the other hand the profound influence of emotion on behavior is generally recognized and appears to be related to diencephalic-cortical discharges (Cannon's 'upward discharge'). The nature of these hypothalamic-cortical relations has been clarified by anatomical studies (Papez [38], Le Gros Clark [39], Ingram [40]) and by physiological experiments. With the latter it could be shown [41] that hypothalamic stimulation results in a distinctive excitatory effect on the cerebral cortex as manifested by the increased rate and amplitude of the 'background' potentials and by the suppression of 'dial potentials' during and following hypothalamic stimulation. These effects became even more marked when strychnine was applied to a cortical area. The firing of cortical neurons initiated by strychnine is likewise increased in frequency on stimulation of the hypothalamus. This facilitatory influence is found in motor, sensory projection and in association areas. The action is bilateral although greater ipsilateral with the site of hypothalamic stimulation. The parts of the hypothalamus which give rise to these phenomena elicit at the same time sympathetic discharges but the cortical activation is independent of the latter and persists also after elimination of the adrenals.

The hypothalamic-cortical relations could be further clarified by the use of the method of neuronography (Dusser de Barenne and McCulloch [42]). Injection of strychnine into the hypothalamus was found to cause first 'firing' (as indicated by the appearance of spikes) of the dorsomedial thalamic nucleus and later of the cortex [43]. This may be followed by the appearance of spikes on the contralateral side in hypothalamus, dorsomedial nucleus, and cortex. It may be assumed that the hypothalamic-cortical pathways just disclosed are utilized for discharges originating in the hypothalamus under physiological conditions. Applying these results to the problem at hand it is suggested that shock treatment consisting of application of electroshock and chemically induced convulsions (metrazol) which lead to increased activity of autonomic centers in general and of the hypothalamus in particular, increase hypothalamic-cortical discharges and cause thereby a change in cortical activity and ultimately in behavior.

Such an interpretation is also applicable to the insulin coma and sleep treatment with this difference, that in the case of these procedures the increased hypothalamic-cortical discharge would result not from direct hypothalamic excitation but, as was mentioned earlier, from removal of cortical control (hypothalamic release). The powerful influence of such an hypothalamic release could be demonstrated by the following experiments [44].

If strychnine was injected into the hypothalamus of an anesthetized cat it led to the appearance of spikes in the hypothalamus while the cortical activity was characterized by grouped sleeplike ('dial') potentials. The hypothalamic and the cortical activity appeared, in general, independent of each other and no synchrony existed between various cortical areas. When anoxia or asphyxia was introduced it was noted, as the cortical potentials disappeared, that synchronous spikes suddenly appeared in all parts of the brain investigated. This discharge, in which the hypothalamus clearly became the pacemaker of brain activity, lasted for sixteen to twenty-five seconds and showed a maximal rate of discharge varying between 6 and 34 per second. It is inferred from these observations that the hypothalamus does not act as a pacemaker of cortical activity as long as the excitability of the cortex is unchanged. However, in conditions such as asphyxia and anoxia which lead to a greater depression of the cortex than of the hypothalamus and therefore to a relative predominance of hypothalamic excitability the discharge of the hypothalamus regulates activity in thalamus, basal ganglia, and cortex, and leads to periods of complete synchrony in subcortical structures and cortex. It is probable that not only asphyxia and anoxia increase greatly hypothalamic discharges but also other procedures such as insulin hypoglycemia and barbiturate sleep in which cortical activity is depressed and consequently the inhibition of the cortex on the hypothalamus is diminished. This interpretation may likewise give a clue to our understanding of the principle involved in narcosynthesis and related therapeutic procedures (cf. Sargant [45]).

Behavioral reactions are best studied in animals by conditioning. Therefore, it was thought of interest to determine whether convulsions or insulin coma modify conditioned reactions. The following procedure was used. Normal rats which jump from one compartment across a small partition to an adjacent compartment in response to a slight electric stimulus applied to the grid of the compartment (unconditioned response) are trained to react in a similar manner to a conditioned stimulus such as a bell or a light. After this reaction has been established it is inhibited by lack of reinforcement, i.e. the conditioned stimulus is repeatedly applied without the unconditioned stimulus. No spontaneous recovery was seen under these conditions but convulsions induced by metrazol or electroshock and particularly insulin coma restored the inhibited conditioned response [46, 47]. This action is cumulative and may in the case of insulin coma lead to a prolonged recovery.The effect of the insulin treatment depends on the number of insulin administrations and the degree of

hypoglycemia, coma being the most effective procedure. If several conditioned reactions are established with this method and are then inhibited by lack of reinforcement in a definite temporal sequence a recovery of these reactions may follow hypoglycemic coma or electrically induced convulsions [48]. This effect of insulin coma or experimental convulsions seems to be specific inasmuch as the restitution of inhibited conditioned reactions is not accompanied by a change in the response of positively established conditioned reactions.[1] The conclusion that shock therapy and particularly insulin coma specifically restituted inhibited conditioned reactions was supported by the following experiments [49] which consisted of two groups. In the first the animals were conditioned, then inhibited by lack of reinforcement and hereafter the degree of recovery of the conditioned reaction on treatment with insulin coma was ascertained. This constituted the first part of the experiment (A). Thereafter the conditioned reaction was again fully established by reinforcing the conditioned stimulus. Then, this conditioned reaction was abolished, not by internal inhibition but by countershock, i.e. the electrical shock was applied to the grid of the two adjacent

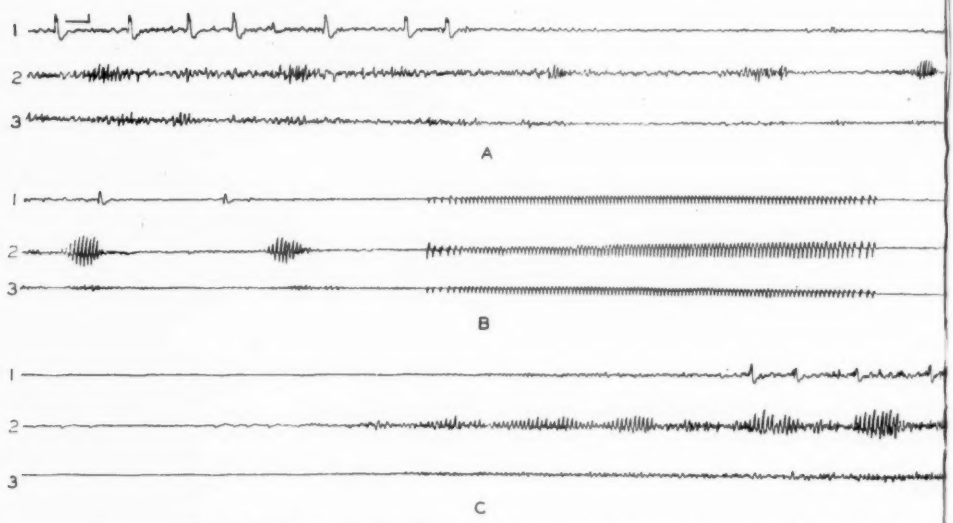

FIG. 1. – Effect of asphyxia on cortex, thalamus and hypothalamus of a cat anesthetized with 'Dial-urethane' (0·45 c.c./kg., i.p.) and injected with 0·01 c.c. 3% strychnine into the right hypothalamus (mammillary body).

Calibration 100 microvolts and 1 second.

(1) Right hypothalamus (monopolar); (2) left ventrolateral nucleus of thalamus (bipolar); (3) left sensorimotor cortex (monopolar). The records A, B, C are continuous. Record A begins 56″ after the onset of asphyxia and shows at the start still well-developed normal and convulsive potentials. Note the synchronous convulsive discharge in B. Immediately after record B was taken air was readmitted. Record C shows recovery in air.

chambers when the conditioned stimulus was presented. The rat jumped, of course, into one of the adjacent compartments and was driven back through the shock into the original compartment. Repetition of this procedure for several days abolished the conditioned reaction completely. Thereafter insulin coma was applied in the same manner as in the first part of the experiment, and the degree of recovery of the conditioned reaction was again determined. This section of the experiment is referred to as part B. The experiments showed clearly that the procedure A led to the typical recovery whereas under B no recovery took place. Apparently the recovery of the

[1] i.e. reactions which had not been inhibited by lack of reinforcement.

conditioned reaction through insulin coma is possible only when this reaction had been eliminated by internal inhibition and not when countershock was the cause of a new learning process leading to a new behavior (avoidance reaction) of the animal.

The last group of experiments was designed to clarify the role of adrenaline in shock therapy. It was mentioned earlier that the sympathetic discharge originating in the hypothalamus and altering cortical activity via the central thalamic nuclei (particularly the dorsomedial nuclei) is considered to be the core of our theory. Consequently, it appears to be on theoretical grounds not feasible to replace shock therapy by the injection of adrenaline. This was clearly stated in my first publication on this problem in 1938[1] [1]. The fallacy of the conclusions drawn by Himwich [3], Cameron [2] and others will appear from the following data:

(1) Stimulation of the hypothalamus leads to bilateral cortical discharges which persist in spite of cervical sympathectomy and transsection of the spinal cord although sympathetic charges to the brain and the secretion of adrenaline are eliminated by the operative procedures (Murphy and Gellhorn).

(2) Rats in which the adrenal medullae have been removed bilaterally show the recovery of previously inhibited conditioned reactions after insulin coma or electric shock in the same manner as normal rats (Gellhorn [50]). Apparently the secretion of adrenaline which accompanies the excitation of sympathetic centers in shock therapy is not essential for the striking behavioral changes described earlier.

(3) Injection of adrenaline was found to be ineffective to restore previously inhibited conditioned reactions although insulin coma and electroshock induced a complete or nearly complete recovery of these reactions [50].

(4) Adrenaline administered in minute quantities diminishes the reflex excitability of the sympathetic nervous system as well as the responsiveness of the hypothalamus to electrical stimulation [4, 5]. Thus, the contraction of the nictitating membrane elicited by stimulation of the mammillary bodies is diminished after injection of adrenaline although the reactivity of this structure to stimuli applied to the cervical superior sympathetic remains unchanged. Moreover, the sympathetic responses such as rise in blood pressure, sweating, and contraction of the nictitating membrane which follow stimulation of the brachial plexus are greatly diminished. Lastly, it could be shown that the convulsive reactions induced by metrazol may be diminished by adrenaline through sino-aortic reflexes [51].

From these data it may be inferred that our theory does not support the assumption that the injection of adrenaline should modify behaviour. Further, it will be noted that insulin coma and electrically or chemically induced convulsions do not act through the secretion of adrenaline. On the contrary it is believed that they greatly increase the reactivity of autonomic centers which in turn may influence the cortex of the brain and possibly the basal nuclei in such a manner as to restore normal behavior. The secretion of adrenaline is but one symptom of the central effect and probably of minor importance in the chain of events which take place in conditioned experimental animals as well as in mental patients subjected to shock therapy.

The investigations may be summarized, somewhat dogmatically, as follows:

(1) Reactions to stress which elicit sympathetic responses in normal individuals are weak in schizophrenics. This suggests that the autonomic (sympathetic) centres are less reactive in this psychosis.

[1]Obviously, epinephrine, which acts peripherally . . . [is] unsuited for this purpose because . . . [it tends] to diminish the central activity of the sympathetic system. The rise in blood pressure due to administration of epinephrine results in diminished sympathetic activity induced by pressor reflexes originating in the carotid sinus and elsewhere in the body (Heymans, Bouchaert and Wierzuchowski). Moreover, even when epinephrine does not increase the blood pressure, it lowers the activity of the sympathetic centers by means of chemoreflexes from the area of the carotid sinus (Chu and Hsu). Quoted from Gellhorn (1938).

(2) Procedures used in the shock therapy of mental disease invariably involve in the experimental animal an excitation of the sympathetico-adrenal system as indicated by hyperglycemia, contractions of the nictitating membrane, rise in blood pressure, sweat secretion, lymphopenia, etc. Hypothalamic and (or) medullary autonomic centers are in a state of heightened excitability as seen in experiments involving direct or reflex stimulation. Chronic experiments indicate that these conditions may persist for relatively long periods of time.

(3) It is suggested that this state of heightened hypothalamic and medullary discharges results from two fundamentally different mechanisms. In the case of insulin hypoglycemia and barbiturate medication (Dauerschlaf) it is the result of disinhibition from cortical control; in the case of convulsions induced by metrazol or electroshock the direct excitation of these centres appears to be primarily involved although the cortical silence following generalized convulsions may also contribute to hypothalamic excitation through disinhibition.

(4) Activation of the hypothalamus, directly or reflexly, is accompanied by excitation of the ipsilateral and contralateral cortex which takes place primarily via the dorsomedial nucleus of the thalamus. This 'upward' discharge occurs also in conditions in which cortical excitability is reduced or abolished and is therefore interpreted as the result of hypothalamic excitation through cortical disinhibition. These hypothalamic-cortical changes are believed to be responsible for the alteration in behaviour patterns which may be seen after successful treatment in clinical cases as well as in experimental animals. Experiments on conditioned reactions before and after different types of 'shock treatment' may serve as physiological models of such changes. It is shown that shock treatment and particularly insulin coma leads to the restitution of previously inhibited conditioned reactions but does not alter the positively conditioned reflexes.

(5) These changes in conditioned reactions occur in normal as well as in adrenodemedullated rats. They cannot be induced by the injection of adrenaline. These facts are not in contradiction with the theory. Its core is not that insulin coma and electrically or chemically induced convulsions act through the secretion of adrenaline but that they greatly increase the reactivity of autonomic centres which, in turn, may influence the brain in such a manner as to restore normal behavior.

(6) Hypothalamic-cortical discharges persist in spite of cervical sympathectomy and elimination of the adrenals and are apparently independent of the sympathetic 'downward' discharge. The latter provides only a convenient indicator of the reactivity of these structures and thereby, indirectly, of the intensity of the 'upward' discharge.

Finally, it should be emphasized that this topic has been limited to the *physiological* basis of shock therapy. Consequently other equally important aspects of this problem have been omitted.

Without attempting to place undue emphasis on the experimental approach to the understanding of a disease entity which cannot be produced in experimental animals it may be hoped that the continuation of this research on a broad basis may not only advance the important field of hypothalamic-cortical relations but ultimately throw some light on the pressing problem of schizophrenia.

Permit me to say in conclusion that I greatly appreciate the honor to speak to this distinguished group of psychiatrists under the chairmanship of Sir Henry Dale whose fundamental contributions to experimental medicine I have long admired

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DISCUSSION

Dr W. MAYER-GROSS (Dumfries) said that it gave him much pleasure to open the discussion after Professor Gellhorn's most interesting and stimulating paper. As a clinical psychiatrist he belonged to those who had been groping in the dark by treating patients without knowing the rationale of what they were doing and hoping that one day some elucidation would come. Now this had been provided by experimental physiology. As a rule physiologists try to avoid the field of psychiatry because psychological complications are not welcome in experimental work. Moreover, Professor Gellhorn from his 'organismic' point of view came much nearer to the approach of the clinician than those physiologists who confine themselves to a special organ

or organ system and its problems. His book had made a great impression on everybody working in this field and it was most interesting to hear from him personally about his latest work.

As a clinician he had certain questions which it was probably presumptuous to ask because they concerned detail which the experiments perhaps could not clear up. Why should it, for instance, be necessary to put the patient into coma, i.e. in a state of decortication, to achieve a therapeutic result? Why is it not possible to stimulate the hypothalamic centres during a mild hypoglycaemia as applied in Sargant's modified insulin treatment? That this is so, seems to prove, he thought, that not only stimulation of lower centres was needed but that the cortex must be influenced directly in order to re-condition it to normal behaviour. How that fitted in with the findings of Dr Gellhorn, he supposed the latter would have no difficulty in answering.

Experiments as described today carried out in animals were hardly possible in patients. On the other hand, people who gave insulin and convulsive treatment every day, like himself, have their patients in a quasi-experimental situation, which was standardized in many respects. The temptation to make use of this opportunity for clinical research in the direction and on the basis of Dr Gellhorn's studies was considerable yet little use has been made of it and very little notice been taken by clinicians of Gellhorn's work.

Dr DEREK RICHTER (Cardiff) asked if Professor Gellhorn could say anything more about the mechanisms by which shock treatments such as an electrical stimulus of the brain, or insulin shock, actually changed the behaviour patterns. He thought the evidence was very convincing of a change in the pattern of reflex behaviour, but how was it that electrical stimulation produced this action on the brain? In considering that problem one could hardly ignore the chemical effects which occurred in the brain as a result of electrical stimulation. These from the point of view of the biochemist were dramatic. There was a loss of something like 70% of the whole brain phosphocreatine content, there was a large rise in lactic acid and there were changes in acetylcholine as a result of ECT (Richter and Crossland, 1949). The normal level showed a sudden drop during the shock followed by a rise, and there was no convulsion until the acetylcholine had risen again: when the convulsions started there was a second drop in acetylcholine followed by a more gradual return to the normal level.

Changes of that kind were suggestive, but on the other hand so easily reversible, so temporary were they, that it was hard to explain on that basis the more permanent effects of shock treatment on the brain. The only clues one had as to what might be happening to the permanent structures were the changes in two other metabolites, ammonia and phospho-lipids. There was an immediate release of ammonia which suggested the possible involvement of the nitrogen metabolism and hence the proteins. There was no bulk change in the lipids but by the sensitive radioactive tracer method changes could be shown in the tissue phospho-lipids as a result of ECT and insulin treatment. This involved one of the more permanent structural elements of nervous tissue: it might offer an experimental basis for explaining some of the changes in the reflex behaviour pattern produced by shock treatment.

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Dr H. WEIL-MALHERBE (Essex) said he had carried out experiments lately on the effect of adrenaline in hypoglycaemic coma in connexion with the observations of Mayer-Gross and Walker who had found that glutamic acid and other amino-acids had the effect of terminating the hypoglycaemic coma. In his view the mechanism

of this effect was adrenergic. To clinch the point he tried the effect of intravenous adrenaline injections. It had been found that rather small doses of adrenaline (intravenous) had exactly the same effect as the amino-acids: they terminated the coma and they caused a similar rise in blood sugar. There were only one or two cases who did not respond and their reaction to glutamic acid was also slight and variable. The point he wished to make was that, however large was the activity of the sympathetic system in insulin hypoglycaemia, the susceptibility to even small doses of injected adrenaline had not been lost.

Dr DENIS HILL (London) thanked Professor Gellhorn for his Address. Largely as a result of Professor Gellhorn's work, some years ago he and his colleagues began to study effects of hypoglycaemia in normals, schizophrenics and other psychotics. The method was to have a standard test and to study the sympathetic-adrenaline responses. A record was made of the changes of the heart rate and palmar skin resistance every 15 seconds, the blood sugar curve was studied in some detail and the effects on the cortex by the EEG from three pairs of scalp electrodes were also studied. It was found that before the sympathetic-adrenaline discharge occurred there was a change in the brain waves, the discharge being seen very frequently within thirty seconds to one minute of this. Within four to five minutes the blood sugar curve rose, indicating the result of activation of the adrenaline mechanism.

In schizophrenic patients the order of these events was variable. What Professor Gellhorn had said was confirmed: there was a diminished reactivity of the sympathetic-adrenaline system in the schizophrenic, that is, the rise in the blood sugar level was delayed much longer in the schizophrenics than in the controls. In many cases of catatonic stupor it did not occur at all. Similarly, in patients with chronic schizophrenia, the brain wave changes were delayed but the order of events for the response to hypoglycaemia, that is, brain-wave change, the sympathetic-adrenaline response, and rise in blood sugar level was varied. In catatonic stupor there was no sympathetic-adrenaline response and no change in the brain waves.

Since the brain-wave changes, which represented depression of cortical function, occurred before the sympathetic-adrenaline response, and since both were delayed in the psychotic group, was Dr Gellhorn certain that the hypo-reactivity of the autonomic centres in psychoses was really what was being observed? Did it not mean that there was a failure, a change in cortical function? Professor Gellhorn had emphasized that there was a sort of balance between the cortex and the diencephalon. The cortex was an inhibitor of the diencephalic release, and Professor Gellhorn had also shown that the diencephalon discharged upwards to the cortex and excited the cortex so that the circle was complete. In these experiments it was the cortex which failed to show the slow waves, it did not show the depression in its functions as measured by the EEG. That was the point which had been reached and the speaker and his colleagues were not sure whether in schizophrenia there was a failure of responsiveness of the diencephalon or some failure in the function of the cortex.

The CHAIRMAN, Sir Henry Dale, said that there were all kinds of questions he would like to put to Professor Gellhorn but he would not delay the meeting by putting them all. There was one central question, which was rather puzzling him, and that was whether Professor Gellhorn suggested that it was the depressing activity of the autonomic centres in the diencephalon which was responsible for the effect on the cortex; and whether, in the hypoglycaemic, and the chemically and electrically excited convulsions, it was the diencephalon and hypothalamic centres which were being directly stimulated. Was it the discharge of the autonomic centres which in turn was affecting the functions of the cortex, or were the functions simply parallel, the convulsive agency affecting both kinds of centres, which happened to be anatomically associated in that part of the brain?

Had Professor Gellhorn any explanation, further, for what these records seemed to suggest, namely, that when the autonomic centres were all under stimulation, whether by hypoglycaemia, metrazol, or by electrical stimulation, the sympathetic peripheral effects seemed to predominate over the parasympathetic? Had Professor Gellhorn any reason to suggest that the sympathetic centres were quicker on the trigger, or more ready for stimulation?

There was the factor of long persistence. Professor Gellhorn showed that some of his effects on the autonomic response persisted for thirty days. Was there any kind of analogy in that with the curative effects of which they had been hearing from their psychiatric colleagues? Thirty days in the life of a rat represented a much longer section of the whole than in the life of a man.

Professor F. L. GOLLA (Bristol) said that like everybody who had worked on neurophysiology in relation to psychiatry he felt stimulated, excited and gratified to hear of the work of Professor Gellhorn. It might possibly interest him to know that, pursuing the lines he had suggested in his laboratory, Dr Ashby had been able to show after the post-convulsive stage, after a series of ECT there was an increase of corticotrophic hormones in the blood. There was likewise evidence of an increase in the gonadotrophic hormones. There were certain other points which were of interest in connexion with Professor Gellhorn's work. Some he must claim to have demonstrated as long ago as 1924 when he was able to show a general slowing up of many forms of activity. Thus the respiratory response to CO_2 was an example of the general slowing of the somatic reactions in schizophrenic patients, as compared with the normal. Similar slowing occurs in gastric secretion, in the specific dynamic responses to food ingestion, and in the blood picture reactions. All these responses eventually occurred but were always very much delayed. That being so, he thought no one could accuse him of not being in great sympathy with Professor Gellhorn. He was delighted with the work he had brought before the meeting, but they were all constantly making the same mistake of over-abstraction when they were considering the functions of the central nervous system. The psychiatrist thought of the functions of the cortex, those who were interested in neurophysiology tended to look at the lower mechanism about which Professor Gellhorn had spoken. There were certain things which seemed incompatible with a primary disturbance in the hypothalamus. Why was it that a disturbed woman got amenorrhoea, and so on? Why was it that a similar disturbance in a man would cause diminution or absence of the libido? Why was it that secretory phenomena were equally affected by disturbance of the brain which was subjected to what they were pleased to call psychosurgery?

Was it not that there was a continual reaction to cortical activity by the hypothalamus, and hypothalamic activity reacted on cortex. In many of the cases improved by physical and surgical treatment he thought that the primary disturbance was in the hypothalamic centres and they had only to realize that any form of disturbance arising from a purely surgical stimulus affected in varying degree the hypothalamic centres. If they concentrated on one or the other they went wrong, in some patients it would be the reaction on the higher centres, in others the lower centres.

In 1894, Chaplin showed that all forms of epilepsy tended to cause a marginal gliosis chiefly affecting the frontal lobe. These observations had been reaffirmed recently. It was quite conceivable that after a series of shocks a cortical change was produced which had its repercussion on the hypothalamic structures. He would be prepared to think that in the cases where there was an absence of hypothalamic reaction, where there was amenorrhoea, absence of gastric secretion, absence of various other visceral responses, that there was organic damage to the hypothalamic region with secondary disturbance of cortical function. In considering ECT they had to account for the fact, not that they had produced a temporary improvement or an

improvement lasting for a day or two, but that they had produced in a great many cases a permanent one. The permanent improvement was generally accompanied by some slight degree of intellectual impairment, and in such cases an operation had been performed electrically on the cortex which, *mutatis mutandis*, was not unlike the operation performed by the surgeons. The patients had been freed from the inhibitory effects of an emotional disturbance possibly by the selective damage done to the prefrontal cortex by the anoxaemia induced by the fit.

Dr H. T. WYCIS frankly admitted that these beautiful experiments had left him somewhat disturbed. If they were to assume that there was depressed reactivity in the hypothalamic mechanisms in cases of schizophrenia, a further depression of the function of these centres should aggravate the behaviour and symptoms. In certain cases of schizophrenia in whom Dr Spiegel and he had performed hypothalamotomy they had made lesions in the posterior lateral hypothalamus and the patients had been distinctly improved. He would ask Professor Gellhorn whether or not he was doing the right thing.

Professor GELLHORN, in reply, said that he was afraid he would not be able to answer all the questions. With respect to Dr Wycis's question it should be mentioned that destruction of the hypothalamus had two entirely opposite effects depending on where the lesion is made. Lesions in the posterior hypothalamus cause somnolence and diminished excitability but lesions in the ventromedial nuclei have the opposite effect (Wheatley). How these results apply to the human is not known, but apparently the hypothalamus is not a uniform structure and the effect of a lesion would produce different effects if different parts of the hypothalamus are involved.

The question of whether in schizophrenia there was a disturbance of the hypothalamus or whether it was a secondary to cortical disturbance was not for him to answer; however, a number of psychiatrists including the late Dr Douglas Singer consistently emphasized the fact (he could never see the clear evidence for it, but that might be his lack of clinical knowledge) that in schizophrenia the primary disturbance was autonomic. Similar ideas were expressed by Ewald, Hoskins, Lemere, Delay, Nielsen and others.

Sir Henry Dale's question as to the causes of diminished sympathetic responsiveness was a very interesting one; its clinical aspects could be answered only by a competent psychiatrist. From the physiological point of view it may be said that studies on rats showed that age was a very important factor in the reactivity of autonomic centers and in autonomic balance. It was found that the sympathetic response decreased with increasing age. Other factors (endocrine activity) might, of course, be of equal importance since some of their earlier work showed that the reactivity of sympathetic centers was increased with thyroid medication and diminished after removal of the thyroid. How long the effect of repeated electroshock on the reactivity of autonomic centers lasted was not determined accurately. Preliminary tests showed that after an interval of ten days the increased sympathetic reactivity persisted. Consequently, in the chief group of experiments the test was performed before and immediately after a series of electroshocks had been given and thirty days thereafter. The latter test showed the reversibility of the effects of electroshock. There were some striking long-lasting effects of insulin hypoglycemia on conditioned reactions which may be comparable to the long-lasting effects which shock therapy may have in the human.

The core of the theory presented was the alteration of central autonomic (hypothalamic) functions as the result of 'shock therapy' and its reverberation on the cortex. This alteration might be the result of release from cortical inhibition under conditions such as hypoglycemia which diminishes cortical activity or might occur from direct excitation of the hypothalamus in electroshock.

The CHAIRMAN, Sir Henry Dale, said that he rather wanted to elicit Professor Gellhorn's view as to whether the centres in the hypothalamus which influenced the cortex were the autonomic centres; he took it that the hypothalamus and the ventricular floor were not one compact functional unit and that they contained nuclei of other functions than those concerned with the autonomic system.

Professor GELLHORN replied that the hypothalamus is often considered to be solely an autonomic structure but that was erroneous; it was based on the fact that from the hypothalamus sympathetic and parasympathetic effects could be elicited. However, even after section of the cervical sympathetics or high spinal transsection stimulation of the hypothalamus continues to influence cortical activity. This latter action is believed to be of great importance in shock therapy. Apparently the neurons of the hypothalamus which initiate sympathetic effects and those hypothalamic neurons which are responsible for the hypothalamic-cortical discharge are anatomically different structures but they undergo frequently similar changes in excitability. Thus, anoxia or asphyxia which depresses cortical functions increases the reactivity of the diencephalic sympathetic neurons [52] and also increases the hypothalamic-cortical discharge (cf. fig. 1). Therefore the reactivity of sympathetic centres may be a fair indicator of the reactivity of the hypothalamus as a whole and consequently of the intensity of the hypothalamic-cortical discharge.

The experiments of Dr Hill were of very great interest because he was using physiological methods to determine the time relationship between hypoglycemia and the sympathetic response and obtained evidence of a diminished responsiveness in schizophrenic patients. He made the interesting observation that the schizophrenic is less sensitive to changes in blood sugar than the normal. These observations based on the EEG suggest a diminished reactivity of the cortex but they do not exclude the possibility that this result is related to diminished hypothalamic-cortical impulses.

Professor Golla's pioneer work, replied Professor Gellhorn, is gladly acknowledged. That sympathetico-adrenal discharges increase the secretion of hormones of the adrenal cortex (via the hypophysis) was confirmed in his own work presented in the main paper. He felt that Professor Golla's observation of disturbances in the sexual sphere (amenorrhoea, absence of libido) in mental patients is quite compatible with the assumption of hypothalamic dysfunction in view of the profound effects of hypothalamic stimulation on gonadotrophic functions [26].

With regard to Dr Richter's question Professor Gellhorn felt that increased hypothalamic-cortical discharges might account for alteration of behavior following insulin coma or electroshock. To link these rather general neurophysiological mechanisms with definite chemical changes in various parts of the brain remains an important problem for future research.

Professor Gellhorn had not made studies similar to those of Dr Weil-Malherbe but would like to mention experiments on rats which were kept in prolonged insulin coma. Injection of glucose failed to restore normal behavior in these animals but electroshock led to restitution of the EEG and behavior even in adrenodemedullated animals although the blood sugar was not raised [53].

Finally, Dr Mayer-Gross had asked why sub-coma was ineffective. Professor Gellhorn emphasized that in his studies on the restitution of previously inhibited conditioned reactions a degree of hypoglycemia which led to diminished reflexes but did not induce coma was invariably ineffective. Here again there seems to be a striking parallelism between experimental results and clinical experience. Apparently in insulin hypoglycemia only a considerable depression of cortical functions leads to a sufficient disinhibition of hypothalamus with consequent increase in hypothalamic-cortical discharges.

[*September 13, 1949*]

FOURTH SESSION

CHAIRMAN :
Professor F. L. GOLLA

PHYSIOLOGICAL PROCESSES UNDERLYING PSYCHONEUROSES

By WARREN S. MCCULLOCH

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I am inclined to sympathize with the good Saint Thomas Aquinas, that patient ox of Sicily, who lost his temper and died of the ensuing damage to his brain, when he met in Siger of Brabant the arch-advocate of two incompatible truths. In his time the schism was between revelation and reason, as in ours it is between psychology and physiology in the understanding of disease called 'mental'.

As we follow down the long trail of neurophysiology from Alcmaeon to Sir Charles Sherrington, we find it leading blindly to the conclusion that 'in this world Mind goes more ghostly than a ghost'. It were tedious to trace the alternative tradition, which begins in Plato's political psychology, conceived in the image of the state to end in Freud's trichotomy of the soul. His epigoni, the latter day illuminati, those new perfectibilians, have dethroned reason but to install social agencies, analytic interviews and transference in the places of espionage, confession and conversion, and fail to add a cubit to our stature. Just as Galileo and the Inquisition were both wrong in the one thing they both believed, that motion is absolute, so these two warring sects both accept as real the separation of body and mind, although there is none in nature. If it were real, it could not be bridged by coining compound adjectives out of 'psyche' and 'soma'.

The real bridge we have is the science of signals, newly developed out of the art of communication. For a signal has a double nature; it is a physical event, which happens only once in a singular world, yet it is essentially capable of being true or else false. Whether the signals are closures of telegraph-relays or impulses in neurons, it is possible for the nets they traverse to have general ideas, in the sense of recognizing universals presented in experience shorn of accidental peculiarity. In recent papers we have shown how nets perform this function in the superior colliculus and in certain parts of the cerebral cortex.

Signal-bearing nets also exhibit purposes in the sense of ends in operation. A purpose is given in any condition of the inputs to a net, such that a deviation from it produces a change in the output that, directly or indirectly, returns into the input so as to reduce the deviation from the chosen condition. In physics, we should call this a state of stable equilibrium. Some circular paths lie wholly inside the nervous system; thus, as cortical excitement increases, the indirect paths returning from it to the thalamus inhibit the further transmission of signals to the cortex. Other circuits go outside the nervous system, but stay inside the organism. This is true of the reflex, defined by Magendie and Bell as a process begun by a change in some part of the body, initiating impulses that proceed over dorsal roots to the spinal cord, whence

they are reflected over ventral roots to the part where they arise, and there stop or reverse the change from which they spring.

In our appetitive circuits, only part of the path lies within us, the rest outside us in the world. These, cast in the molds of our ideas, mark out what we call purposive behavior. They are error-operated, driven toward their goals by some measure of the difference between the end and its attainment. It is the same device which the engineer uses routinely under the name of a *servomechanism*, whenever he wants to embody purpose in a machine. It would be strange indeed if he, himself, worked on a very different principle.

As psychiatrists, it is natural for us to try to carry the analogy further. If animal and machine operate in the same way, they ought to suffer from some of the same diseases, or *gremlins*, as the engineer calls them, namely, the ones common to all circular mechanisms. The diseases of such systems, the gremlins, defy dimensional analysis. Energy, time, and length are not their measures. Pure numbers and the logarithms of numbers are but the ground on which they figure. At the moment, I am not concerned with finding out their precise anatomical location. The properties of nervous circuits are greatly affected by changes in quite different ones which may have a part in common with them. The central nervous system performs nearly all its operations many times over in parallel, and proceeds to the next step according to a general agreement of its signals. If one part is disordered or preoccupied, it performs the same function elsewhere. Of the input it receives, it filters out and discards all but one part in 10^7. It is not surprising that it should defy the best neurologist, for all but the grossest defects. That is their misfortune and not yours.

On more than one occasion I have said, not quite in jest, that in their essence gremlins and neuroses are demons, sentient and purposive beings, exercising in their own right properties more mental and more physical than any psychoanalyst has yet had the courage and clarity to claim for them, as much when they haunt machines as men. I speak tonight of the nature of demons.

Half-way between the inner feedbacks of the brain, whose diseases are convulsions, tremors, and rigidities, and those outer, appetitive disorders that frequent the public world, be they 'isms' or neuroses, there is one particular demon I shall describe at length, partly because he produces wellnigh intolerable suffering, and partly because his ways and doings are better known than those of any other. He is called *causalgia* – burning pain. I do not say this demon is all soul, though you will find him embodied now one place and now another. To torture us at all he must exist somewhere, somehow, as a perversion of some function in some nervous structure.

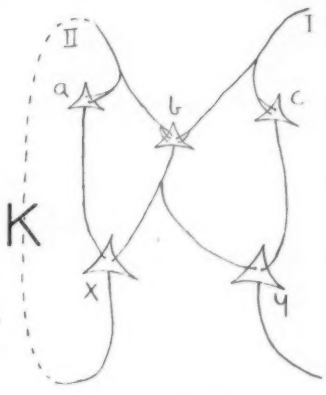
Causalgia begins as a perversion of a reflexive circuit. If you thrust a hand into hot water, or into water so cold that it seems to burn, the sensory receptors for pain and extreme temperature are excited. Their impulses, coming by fine fibres of the sensory roots to their own segments of the cord, excite the small internuncials that play upon preganglionic neurons of the sympathetic system. These, in turn, excite the sympathetic ganglia whose axones, running in mixed nerves and plexus about blood vessels, descend to the burning hand. Their barrage shunts the blood from the skin through the muscle and the bone, thereby conserving temperature within by decreasing the thermal conductivity of the skin. To maintain the proper temperature of the affected part is the function of this reflex. Its perversion is causalgia.

Let us see how the perversion happens. We used to demonstrate by placing a clamp upon the left internal mammary artery how changes in the circulation of a portion of a nerve may alter its excitability: for then the left phrenic nerve responds with a hiccup to the heart's electrical systolic pulse. We are all familiar with the paraesthesia and the cramp that comes from sitting on the blood supply of the proximal portion of the sciatic nerve. The standard history of causalgia is injury to nerve sufficient to damage, but not to sever it. Thereafter it responds to almost anything

In 1944, Granit stimulated the sympathetic fibres to a limb of a cat, and recorded the afferent impulses from it to the cord, before and after crushing the mixed nerve. The experiment is easily repeated, and the outcome what you would expect: only after the injury, a volley of impulses over the post-ganglionic sympathetic fibres provokes a volley returning by the dorsal root. From what we know of cross-talk of signals generally, we should expect coupling to occur principally between conductors of comparable resistance and capacity, and, consequently that sympathetic efferents, being fine fibres, would excite fine-fibre afferents reporting pain and temperature from the peripheral distribution of the affected nerve. We do not need to jump from fibres to sensations, or from cats' brains to men's. Earl Walker, in curing causalgia of the arm, cut all preganglionic fibres of the cervical sympathetic chain, leaving the peripheral connexions intact, and delivered the chain itself into a glass tube through the wound. The patient, on coming out of anaesthesia, was without his pain; but for several days, as long as the ganglia were still somewhat alive, stimulation of the chain evoked again the burning pain in the old place.

This, then, is how the reflex was perverted. Injury to the nerves permitted cross-talk from the post-ganglionic sympathetic nerves to the nerves reporting burning pain. This is a vicious circle. Efferent impulses which should have decreased the number of afferent impulses have increased their number. The reflexive circuit has become regenerative. This is a self-perpetuating active memory projecting the pain upon the peripheral distribution of the afferent nerve that it invaded. When the injury is recent, and the nerve healing well, causalgia may be terminated by temporarily blocking the reverberation in any part of the closed path. But if the wound remains an artificial synapse, the trouble starts again. What is far more interesting is that sometimes simply blocking the nerve distal to the lesion relieves or terminates causalgia, for this bespeaks the role of other afferents in maintaining a background of activity in the internuncial pool.

Now the patient keeps his white and glossy hand moist and cool, for every jolt, touch, rub, or tickle turns to burning pain. How came this perversion of sense? Strike the back of your hand against your chair and attend to the sensation. There is first a quick pain carried by fast fibres, then the late burning pain which comes by the fine fibres slowly to the cord. Whenever we do anything vigorously, these impulses are present, but the faster tactile or proprioceptive fibres get their impulses first to the cord, where they determine the pattern of internuncial activity before the impulses for burning pain arrive. In causalgia, the story is reversed. The painful impulses are always there, and all other impulses augment the process already under way. Here is Gasser's diagram of how such things can happen. Suppose the threshold of each neuron is just two synchronous impulses upon it. Then afferents of system *I* will fire *b* and *c* in phase and these will converge on *y* to fire it. But now let *II* get under way, and *b* will be swept into phase with *a*, convergence will occur on *x*, and it will fire. If this happens, the threshold of *b* must rise until *I*, which has but two synapses upon *b*, will become unable to fire *b* at any time. *II* has stolen the necessary internuncial *b* from *I*. But in causalgia, *x* feeds back to *II* and shuts *I* out forever. Obviously the scheme is oversimplified. *I* has many synergic fellows, and if enough of them can be got going at a time, they may be able to steal *b* from *II* and so



Gasser's diagram

break up causalgia. Among the best results that I, myself, have seen in the treatment of causalgia are Livingston's cases, in which good surgery of the wound was combined with early consistent and powerful persuasion to make use of these other afferent paths. He provided his patients with a whirlpool, into which they could put the painful part while they, themselves, controlled its rate of stirring. Those who were able to get other sensations through their burning pain usually recovered without further surgery. Here, at the reflex level, a kind of psychotherapy, by which I mean a use of afferent channels adequately stimulated, has exorcised the devil.

Unfortunately, if we wait too long, this method, as well as temporary and permanent nerve-blocking and section of the dorsal roots and section of the sympathetics fail, for the devil has moved into the cord. That he has not yet gone higher is clear; for spinothalamic section at that time will shut him out of our heads. I remember such a case after bilateral tractotomy and blocking of nerve proximal to the lesion. His affected foot was still obviously the recipient of a sympathetic barrage, which could come from no other thing than persistent activity reverberant in the cord. At this stage, instead of cutting the spinothalamic paths, the limb may be cut off – I have seen it done only too often – and it but substitutes a painful phantom for the real limb whereon the pain was formerly projected. This state has been imitated in experimental animals by Dr Margaret Kennard, who injected alumina cream into the sack around the cord. This produces no lesion apparent grossly or microscopically with ordinary stains. Yet the beast behaves as if he had causalgia of the corresponding regions.

Finally, there comes a time when section of the spinothalamic tracts is of no avail: the devil has moved upstairs and is reverberating there. Here we are confronted with new difficulties, for lesions dissociate aspects of pain, which, to the normal man, seems an elementary sensation. As the spinothalamic tract passes through the mid-brain, fibres leave its main stream, and passing medially, terminate among the cells lying between the periaqueductal grey matter and the deepest layer of the superior colliculus. Mid-brain tractotomy at the level of the inferior colliculus prevents all pain and suffering; whereas, at the level of the superior colliculus, although the sensation of pain disappears, the suffering is as great as ever. In such a man, I am told that noxious stimuli produce suffering, fainting, sweating, and pupillary dilatation as if nothing had been done to interrupt their paths. The ascending spinothalamic tracts play into appropriate portions of the thalamic nuclei, whence relays extend into the cortex devoted to corresponding portions of the body. What is most important here is that in some cases of causalgia and of painful phantom limb, stimulation of the proper part of the postcentral convolution is sometimes perceived as pain. Among these cases are the few who seem to profit by excision of that part of the cortex. It seems unlikely that this cortex is part of a closed path through which the demon rings his changes. More probably, the improvement in these patients resembles the one achieved by peripheral block, and the cortical area in question only contributes to the sustaining excitation.

Finally, lobotomy, which has removed neither the sensation nor the primary affective component in any case that I have seen, does prevent the agony of worrying that makes distress a part and parcel of the typical character of such a patient. Only in this sense does the causalgia matter less to him, that he minds it only when he feels it. It may well be the demon haunts these cerebral paths, but they are certainly the last place where we ought to try to break his circle. I strongly suspect we shall find his last retreat in a certain small region of old and ill-defined structures near the core of the neuraxis, that stretch through the mid-brain and the thalamus. For lesions here affect the very springs of caring and of mattering. With this region left intact after all in front is gone, animals still learn, to the extent to which, without a cortex they can have ideas and control their movements. Whereas, with large lesions

here, all else intact, they bother little if at all to respond, and do not learn.

Let us consider the demon from a slightly different point of view. Gasser's diagram represents the normal condition also, as long as we take the circuit *K* to be degenerative. In that case a certain fraction, smaller than unity of the afferents in *II* is fed back to them by *K* and subtracted ; this process keeps up until the circuit has come to rest at a definite level of activity directly proportional to the original input from *II*, if less variable than it. This level of activity is transmitted upward from *x* to communicate the sensory information from *II*; similarly from *I* by way of *y*. In causalgia, where *K* is regenerative, any input from *II* is amplified and added to itself, not subtracted. The level of activity in *K* then grows geometrically, until it is bearing all the activity it can bear; in this state it remains, to decline very slowly by attrition of fatigue. No matter how small the primary input, as long as there is any, the output is always the same: the maximum possible at *x*. The same thing happens if it was a collateral input, say from *I*, that triggered *K*. Furthermore, the proper response *y* from *I* will usually be prevented, either by Gasser's effect, already described, or else by direct inhibition from *x* when the latter is greatly excited. In the affected part the causalgic cannot distinguish among heat, touch, and pain, nor can he tell a greater degree of one of them from a lesser: in every case he experiences only the maximum of burning pain.

In this way the demon, causalgia, suppresses practically all the information formerly transmitted over *II* and every other circuit even partly connected with it. He does it by a kind of imperialism, substituting his own characteristic, repetitive, stereotyped, impertinent response for a whole range of infinitely varied and subtly adaptive responses to the actual facts of the situation. As we have seen, he takes time to get himself ingrained, like a skilled act. Thereafter he moves in on us, no longer requiring for his maintenance the particular structures from which he sprang.

These properties together describe more exactly what Lawrence Kubie has called the 'repetitive core' of every psychoneurosis. The difference is that the latter begins elsewhere, in the appetitive circuits.

In common with other psycho-analysts, Kubie makes a sharp distinction between processes which are conscious, and others which were or might have been conscious, but are now shut out of consciousness. In the latter he puts the core of the neurosis. Now the psycho-analytical use of the term unconscious, if somewhat indefinite, is quite a special one. In essence, I believe, it is nothing but the supression of information as we have just described it. The memories and learned reactions subserved by circuits connected with the regenerative circuit can no longer be evoked, not because anything has happened to them, but simply because all the stimuli which once evoked them, feeding secondarily into the regenerative circuit, now produce only the invariable neurotic response, which displaces all the others. In effect, such memories and such learning become inaccessible, although they return as soon as the circuit ceases to regenerate. The process looks like an active repression, particularly when combined with the secondary effect the psycho-analyst calls resistance. A man usually finds the output of the regenerative circuit disagreeable, so he learns to avoid stimuli which feed into the circuit in any way, as well as situations where such stimuli are probable. Thus the causalgic guards his hand even from his doctor. This development may go extraordinarily far.

But in some respects the psycho-analyst's metaphor is misleading. We cannot say the neurosis, or its root, is 'walled off' from the rest of the organism – quite the reverse. The regenerative circuit pours its output into other structures very strongly and usually distressingly. Again, it is only too easy for impulses from elsewhere to trigger the circuit and produce its characteristic maximal output. But that is all they can do: they cannot make it do anything different, they cannot stop it once it has started. We may say the neurosis is autonomous, almost completely so; it is not isolated.

So far I have spoken of the invasion of demons. But they can go outward and overwork a reflex path until its effectors or receptors are distorted or destroyed, as in *pruritus ani* and in gastric ulcer. I shall give you a different example because my knowledge of it is first hand. Franz Alexander became interested in a group of erstwhile energetic people whose living is crystallized about some goal made unattainable by Fate. Thereafter they do their daily chores without zest. They are always tired. A few hours after eating they feel faint, warm, and sweaty. They eat too much and sleep too much and turn their food to fat. When Alexander came to me, he and his friends, following Szondi and Laz, had studied the glucose-tolerance curves of these people and found them abnormally low. What he asked me was whether these patients suffered from an under-activity of the sympathetic system or an over-activity of the parasympathetic system or both, for he knew that atropinizing the patient prevents the weariness and the postprandial faintness, although it does not restore the zest. For this reason he names the condition 'vegetative retreat'. So far our studies of their sympathetic system are far from complete; but of an excessive vagal excitement of the pancreas there can be little doubt.

Reliable statistics have shown us that neurotic patients are significantly more sensitive to insulin than is normal for their age and diet. Not so Alexander's patients. In their cases, to account for the increased speed of removal of sugar from the blood and the abnormal smallness of the final values after they receive sugar by vein, one must suppose an excessive secretion of insulin caused by excessive vagal excitation of the islands of Langerhans. Thanks to DeWitt Stetten, there is an easy way to check this; for he showed that with an excess of insulin, water made with heavy hydrogen, given concurrently with glucose, left heavy hydrogen in the fatty acids that are then produced because the patients turn their foods to fat. The odds are many to one that, on receipt of sugar, though their body temperature remains constant, their uptake of oxygen declines by an amount proportional to the amount taken from the sugar as it goes to fatty acid. If all of the sugar we injected went that way, we might expect a fall of 50% in oxygen uptake while the sugar was disappearing from the blood. In these patients we encountered falls as great as 30%, meaning 3/5 of the sugar went that way; in a normal man there is no change.

Let me rehearse, then, the doings of this devil. Springing from the tedium of life, he has produced an exaggeration of anabolic processes to a degree which has actually enfeebled his host and only fatigued him the more, thereby preventing him from developing a luxury of energy sufficient to extricate himself from his intolerable plight.

At this point I ought to hold my peace where I would in all conscience admit my failure and cry for help. For years I have tried and failed to find out how the brain knows how much sugar is in the blood; all I can be sure of is that it tastes it in some place other than the brain, for I can fool it. For years I have been trying to find all the ways by which the brain affects that quantity, but one eludes me. For the brain can still control blood sugar when the pituitary is removed, the vagi cut, the spinal cord transected above the topmost outflow of the sympathetic system. So much for my incompetence.

Causalgia exemplifies two modes of transition from an inverse feedback to a regenerative action. It begins by an injury which is equivalent to throwing a switch that reverses the sign of the feedback from negative to positive. Its ingression into the spinal cord is equivalent to a change in the ratio of output to input, or gain, of an amplifier, which overloads it. This change in gain is obviously the result of oft-repeated over-activity in the circuit. Now, in general, gain depends upon frequency. For a circuit whose action is inverse at the frequencies it is intended to handle, there will exist certain other frequencies, higher and lower, for which it is resonant. To be alerted to anything is to increase the gain in some circuit. If this circuit is excited

at a frequency for which it is resonant, great overactivity can be produced, and like causalgia in the cord, may permanently augment its gain, so that it goes into self-sustained activity.

Telephone switchboard operators used to be subjected to a signal alerting them to plug in a line, ask and hear a number, make a connexion, and listen until they hear both parties speak, cut themselves out of the circuit, and stand by to receive the next alerting signal. Lively girls of high intelligence, doing this at busy switchboards, became tense or nervous, had rapid hearts, sweaty hands, and nightmares. This form of nervous breakdown became a serious industrial hazard, requiring months of care in a sanitorium. The expense to the company was great enough to prompt the development of the dial system.

This genesis of neuroses has been studied thoroughly in sheep and goats by Liddell. These beasts respond by lifting the fore-paw to a barely perceptible electrical shock. If the stimulus is repeated at equal intervals of one or several minutes, the sheep soon gives the response at the proper time, even if a single stimulus is omitted. That is all that happens. If he is taught that the beat of a metronome at one per second is followed by the shock, he tilts and raises his head and pricks up his ears whenever he hears the click, and may even raise his leg before the shock arrives. He can be taught to respond similarly to touch or sight instead of sound as the alerting signal. This is neither a painful nor a distressing experiment, nor one in which there is any task to require a difficult discrimination. Nevertheless, if the signal and shock are repeated at intervals of one minute or of four minutes, the beast becomes neurotic. With the shorter interval, he stiffens the fore-limb, breathes slowly, has a slow pulse and somewhat narrower pupils. With the longer interval, he begins to shake or paw with his fore-limb, pants, has a fast pulse and dilated pupils. Once firmly established, by a few runs each day for a few weeks, the reaction becomes so fixed that it lasts at least five years without reinforcement. Moreover, the beast ceases to be normally gregarious, and his fast irregular heart and respirations and much moving about continue permanently, even during sleep. Obviously the frequency of stimulation determines not only the existence of the neurosis, but also whether the sympathetic or parasympathetic system is the one involved.

Beside the neuroses that are generated by repetitive experience, there are some which clearly spring from a single, intense psychological insult. I have in mind what the American Army calls 'Blast'. A man near an explosion, but not so near as to suffer organic damage to his brain, starts to run in frenzy. After being stopped, say long enough to smoke a cigarette, he has lost all memory of the events from just before the blast until he smoked the cigarette. Thereafter he is startled easily, is terrified by the sound of airplanes or the back-fire of a passing car, and dreams of battle frighten him. He comes to resemble a hound gone gun-shy. From Walker's work we know that acceleration of head as great as in these patients produces throughout the central nervous system, an electrical disturbance which resembles that recorded in an epileptic fit. The blast itself can never be recalled. Again, the neurosis is an active reverberation, as shown in the autonomic outflow and the dreams. Why a single blast is able to set up such a process is not obvious. One would naturally suspect that the applied force, rather than the host of simultaneous signals over many nerves, was the cause, except that similar pictures appear in men too far removed from the explosion; merely as a consequence of seeing and hearing their companions killed in battle. Things of these kinds have easy access to a kind of memory other than either of those apparent in causalgics, neither mere reverberation nor the one that mediates our oft-repeated acts, but the one that stores our glimpses of the world, making it seem like a pack of photographs of things that happened once. Here each attempt to look again at these horrors, or anything that might incite him to revive them brings back the frenzied fear. The content of these snapshots is not itself the

fear, and if the fear could be forestalled, they could be seen for what they are.

I do not know when first man had it in his power by drugs to quiet these churning fears. In our Civil War, the patients were made drunk, and, as they sobered, were allowed to relive and discuss the things that racked them most. But we forgot the art of treating them, and re-discovered it in our war with Spain, when it was christened Hypnotic Therapeutics. In World War I we learned it once again, this time with ether, and in World War II barbiturates came into vogue, under the name of Narco-analysis or Narcosynthesis. Next time, if there must be a next, I hope we have the grace to acknowledge the good works of our forebears, and have the skill to stand upon their shoulders.

To my mind, Fabing's trick[1] of following amytal by coramine seems an improvement, at least statistically in its results, and scientifically, for, inasmuch as the bulk of his patients lost their terrors and their amnesia without analysis, synthesis or intentional suggestion by any fellow man, his success ought to be attributed to the sequential action of these chemical agents on the central nervous system. The amytal brought many processes to rest; a violent reliving of the accident ensued, and this was suddenly converted to the waking state by the generalized excitation of the brain by coramine. Fear was swamped out by normal activities, among which were the memories themselves of the accident, now quite innocuous.

For all our hypotheses, of the majority of neuroses that begin in civil life, the origin seems to me undiscovered – probably undiscoverable. But the history of any case suggests that early in the process they may be broken up as easily as if they depended for their existence upon little more than mere reverberation, and only later became so fixed as to start up again once they are stopped.

Another origin of neuroses is instanced by conditions in which the gain is increased by the sudden withdrawal of various things, usually narcotic or soporific to the nervous system. I do not mean the convulsion that not infrequently follows the withdrawal of barbiturates. I am thinking, first, of the jitters of the alcoholic who tries to stop, and becomes unable in his tremor and terror to lift a glass to his mouth; second, of the violent autonomic discharge that ensues when morphine is withheld from those physiologically addicted, including the decorticated dog; and last, that all-pervading anxiety which comes when we lose the most wholesome of soporifics, a convivial bed-fellow. Fortunately, thanks to your British drug, myanesin, these problems have become simply and safely manageable. Henneman in our laboratory has most elegantly demonstrated that myanesin will prevent the activity of internuncials necessary for multisynaptic arcs, including the nociceptive flexion reflexes and the facilitation and inhibition produced by direct stimulation of the reticular formation of the mid-brain and hind-brain or by torsion of the head on the trunk. It was these experiments which led Dr Cooke to suggest trying it against the overactivity of masses of small cells produced in the aforesaid withdrawals, and so to experiments at Manteno State Hospital on large numbers of patients with sympathetic symptoms.

I have purposely dodged the term 'anxiety'; for it is now applied to any state of the central nervous system giving excessive sympathetic activity. I have already described three such states, which are clinically and experimentally distinct: the first induced by repetition in telephone operators and in sheep, the second by single fright in a blasted man and gun-shy dog, the third by withdrawal of certain drugs in man and dog. All three conditions show exaggerated startle, and respond, at least temporarily, to myanesin. A good instance is my old dog Puck, who was early frightened by fireworks. Every thunderstorm puts Puck into a state of terror: he shivers continuously, hides under the bed, and refuses food for many days. The slightest stimulus startles him. Myanesin will not prevent thunderclaps from frightening him, nor does it completely suppress the startle; but after the storm passes he eats, and instead of hiding, comes to be petted without shivering. Myanesin has evidently damped the

[1]Fabing, H. D. (1947) *Arch. Neurol. Psychiat.*, **57**, 14.

regenerative process. In the remaining case of the sheep, experiments with myanesin are now under way, although we do not yet know the results.

Besides all these, there is a fourth condition like the apprehension felt by a man about to visit the dentist, except that it often wants any well-defined object. The sympathetic system is evidently overactive, but mere noise will not augment its output further. The man shows no great exaggeration of startle, and his feelings are not much affected by myanesin, although his sympathetic output may decline a little. Masserman's cats appear to furnish the corresponding condition in animals. They are put into the ordinary experimental set-up for conditioning, where they learn to perform some response rewarded by food. Thereafter, when they perform the response, they receive instead of the food, or accompanying it, a blast of air in the face, like a cat spitting. Such cats will not eat, fight against being put into the conditioning box, and become unsociable. But they have no exaggerated response to startle, do not increase their sympathetic activity in response to noise, and, as I have just heard, are not measurably affected by myanesin. They seem anxious–but I suspect their apprehension is more like that of the ordinary neurotic patient.

Every treatment of causalgia has its counterpart in handling neuroses in general, at the proper stage. But, at the moment I am chiefly interested in one resembling the newest treatment of blast. We have had nearly five years' experience with it to date. Of the first 117 whose treatment ended some four years ago, 79 are still well today, and 2 who relapsed have recovered on repetition of the treatment.

For its rationale let me recall to you Gasser's diagram when the circuit K is regenerative. If we raise the threshold of *b*, we shall be able to halt the reverberation temporarily. When the threshold falls again, the normal input *I* may be able to pre-empt the necessary common internuncial, so *II* will not get going as before. Whether this happens depends upon the exact times at which signals from *I* and *II* arrive. A second way of doing this would be to make *b* temporarily indefatigable; for then *I* could fire it at any time and be on an equal footing with *II* in the race for possession of *b* at every round. A third possibility lies in the background of excitation and inhibition, not indicated in the diagram, but always there in the living nervous system. For, any shift that might fail to excite *II* or inhibit it or do the reverse to *I* might upset the balance. In fact, merely to excite both maximally or inhibit both maximally would tend to equalize their chances for possession of *b*.

Lorente de Nó has shown that CO_2 raises the voltage and threshold of all axones, and also, what may be most important here, it renders them almost indefatigable. The effect of this on the activity of various structures is diverse. The cortex, normally so far from fatigue as to be capable of an epileptic discharge whenever it is electrically excited, has its normal level of activity controlled by inverse feedbacks which keep its afferent impulses down to a small established average. Consequently, the effect of CO_2 on fatigability is here without effect, but the rise in threshold it induces puts a stop to cortical activity. In the respiratory mechanism the opposite is true, for its fatigued neurons are always the recipient of more impulses than they can relay. They are too tired to have a convulsion, no matter how frequently we excite them electrically. CO_2, by raising the threshold, can make little difference, but because it also prevents fatigue, it will cause a vast increase in respiration. Other structures of the thalamus, mid-brain, and hind-brain exhibit intermediate conditions.

Whether this is the complete story, or whether there is also a chemical specificity, remains to be proved. At the moment, we can only add that respiration of 15% CO_2 in O_2 prevents the seizures normally induced cortically by electrical stimulation or by metrazol or similar substances, whereas it augments the effect of bis-beta-chlor-nitrogen mustards, which start fits in the hind-brain, notable in the cerebellum. It follows that the respiration of 30% CO_2 in O_2 will alter, briefly but extremely, the background of excitation for neurotic reverberant feedback loops, and for normal

inverse ones. This alteration may halt reverberation. Over and above this shift, by rendering *b* indefatigable, CO_2 gives *I* and *II* equal chances for the necessary internuncial; in some of them *I* will succeed.

In giving, say forty treatments of say forty respirations each, of 30% CO_2 in O_2, one cannot avoid the suggestive effect of a doctor, a nurse, a mask, and submission to transient loss of consciousness. Still, in view of our contagious incredulity, particularly in the first series, the score is too high to attribute to psychological factors. Others now have longer series and better scores than we. In fact, their enthusiasm is somewhat alarming – particularly their reported success in treating gastric ulcer. I have been most surprised by the results in disorders of speech, commencing in childhood and treated in the twenties or late teens. If we exclude stutterers – the people who say I did – – I did – – I did – – etc., who often have additional signs of damage to the brain, such as an arm that fails to swing normally in walking, or too fixed a stare – and accept only stammerers – those who say I – – – – – – – – I did it – then, of 50 cases the successes numbered more than 25. Having seen my sister, a teacher, and my cousin, a surgeon, bring on stammering by learning the one to write, the other to shave with the left hand, I am not altogether satisfied with supposititious psychic skeletons in the unconscious. It is enough to know that the devil is a reverberation who succumbs to CO_2.

Unfortunately causalgia and great anxiety are prepotent demons. Under CO_2 they are intensified, as if fatigue alone had limited their sway. The patient never leaves the doctor long in doubt on this score. He simply refuses a second or third treatment.

Beside prepotent demons, there is another condition that resists – or is unaffected by – CO_2. I hesitate to speak of anankastics – obsessive or compulsive – again at this meeting. The only experiments that have produced a condition which may be compulsive are Kurt Richter's on rats, poisoned once severely and thereafter required to select their diet from samples of various foodstuffs, of which, now one now another contained a little of the odorous poison. They hang on to the wires of their cages, wrap their tails around a wire and, even in sleep, hang on as if this would insure their not eating the poison in a moment of relaxation. This behavior persists for at least sixty days when the poison is withheld. If a similar picture can be produced in primates, we may be able to work out the complete circuit. In man mayhem must be less radical, but obviously there has been enough of it already to show that some portions of the fore-brain contribute to or constitute the closed path, or reiterative core, of obsessional stereotopy. I only hope that while neurosurgeons still have the operations on their consciences, psychologists will have an opportunity to study the way leucotomy, topectomy, and thalamotomy destroy the force, and finally the ideas, of those troublesome sentiments, for until we know more than we do today of the nature and boundaries of the consequent psychopathy we are in danger of robbing the patient of some of the ends of life which make it in the long run socially worth while.

Discussion

The Chairman, Professor F. L. Golla, said that there was one point which struck him and that was whether a mechanistic approach to the neuroses was a possibility. Somewhere about 11 o'clock at night, standing in one of the highways, one would see a lot of people passing along in a great variety of moods; it was the hour at which the public houses closed. He could not think that very much would be learned from the sight of the effects of the poison but from the fact that each had a different system, a different stratum at which the alcohol worked. Professor McCulloch might be asking too much, it might be that they would ultimately have to correlate the mechanistic account with introspection to make it intelligible. As living beings they could do something which no mechanical thing could ever do – they could objectify themselves.

Dr DEREK RICHTER wished to pay a tribute to the most erudite and stimulating account which Professor McCulloch had given. Professor McCulloch had described, particularly in his writings and to some extent in his Address, the electrical mechanisms in the brain, and he would like to ask if there was any recent evidence of an interrelation of the electrical rhythms of the brain and behaviour at the higher levels. The previous work by Adrian and the work done in the Burden Institute were a little disappointing in that they showed a negative rather than a positive relationship between the electrical rhythms which one could pick up and actual behaviour. It was known that the *alpha* rhythm disappeared if conscious behaviour was started. They had been particularly interested in that problem at Cardiff and had recently been working on the relations between the actual phase of the electrical rhythms and behaviour. Some of the evidence might appear to give confirmation of the views of Professor McCulloch. The actual effect which he wished to mention was the relation of the phase of the *alpha* rhythm and the moment of initiation of a voluntary movement. The *alpha* rhythm could be shown very easily in an individual who was sitting relaxed with closed eyes, and the moment when he initiated any voluntary movement appeared to bear a relation to the phase of his *alpha* rhythm. Every tenth of a second the probability of his starting a movement increased, showing, in effect, a working relation between one of the rhythms and psychomotor behaviour (Kibbler, Boreham and Richter, 1949).

Was there any other evidence which would point to an active relationship between the rhythms rather than the negative type of relationship which had generally been described?

REFERENCE

KIBBLER, G. O., BOREHAM, J. L., and RICHTER, D. (1949) *Nature*, **164**, 371; Reports of 2nd Internat. Congress of EEG (1949), Paris.

Dr DENIS HILL thanked Professor McCulloch for a most interesting Address covering so many fields in which they were all concerned. He was surprised to hear him use the word 'demon' in describing the development of neuroses. He referred to reverberating processes of activity which might move towards the cortex and he referred to the state for such reverberating activity as the demon: 'the demon moves'. Keeping to his mechanical terminology it seemed to the speaker that Professor McCulloch was suggesting that the attention of the rest of the brain was directed towards the movement and activity of this electrical 'demon'. If that was so, there was a lot left after the reverberating circuit was accounted for.

Dr D. A. POND (London) said with reference to the idea of feedback, it was clear from Professor McCulloch's talk how nerve injury could produce 'cross-talk' and positive feedback in cases of causalgia. However, it was not clear what was the analogous explanation for the development of positive feedback mechanisms in the C.N.S., where there was no evidence of structural damage. The concepts of circular reflexes, the laying down of new pathways, etc., had a long history in psychology and physiology, and he was not clear how far Professor McCulloch's description of positive feedback as a functional disturbance in an electronic machine, threw light on what were the possibly comparable disturbances in the nervous system in cases of mental disorder.

Dr F. A. PICKWORTH (Birmingham) had studied the nature of nervous processes in mental disorders, and in this had profited much by reading Professor McCulloch's publications.

He (Dr Pickworth) wished to distinguish between mental and neurological processes. As far as the mind was concerned there was plenty of evidence that the central nervous system was not the 'master tissue' of the body. For example, the brains of schizophrenics were in his experience often better structurally than those from non-mental cases. Schizophrenics could be taken as typical since they occupied half the mental hospital beds throughout the world. Freeman [1] applied the terms 'particularly normal'

to such brains. Dr Pickworth had known intimately several persons whose minds and personalities were not grossly altered by large cerebral destructive lesions. He had seen in Institutions, quadriplegic idiots who had minds and even characters of their own, although handicapped in the development and expression of them. Cerebral stimulation can restore function in long-standing mental abeyance, which fact establishes the integrity of the subservient central nervous system. The conditioned reflex, contrary to general acceptance, was not typical of a mental emotional state, since so much automatic (robot-like) behaviour was devoid of mental-emotional component. Attempts to identify unity of mind with the paired structures of the central nervous system were therefore doomed to failure. By contrast, all intense mental-emotional processes were regularly accompanied by vascular changes in the body. Corresponding mental changes were to be noted with physiological changes of blood pressure, which altered the local cerebral blood flow. Similar changes of both could be induced with drugs, toxins, or hormones acting over a period of time. He had been able to show, by a specially devised staining technique, structural alterations of the cerebral blood flow in cases of mental disorders. These changes were very evident in early general paralysis. The lantern slide shown indicated clearly congestion and gross structural lesions of the cerebral blood vessels of the motor cortex. He believed that, if cerebrovascular lesions were accepted as the pathogenesis of general paralysis, one could apply Osler's dictum of 'know syphilis in all its manifestations and all things clinical shall be added unto you', to other mental diseases, including the psychoneuroses. The aetiological agent may differ, but the pathogenesis is the same, namely pathological deviations of the local cerebral vascular flow, details of which are given in a pending publication [2]. The dependence of reflex nerve function upon the local blood flow was first shown by Sir F. W. Mott [3]. The blood flow abnormalities in schizophrenia have been likened to ergot poisoning. Those in early and late encephalitis are readily demonstrable, and in his opinion easily correlated with the sleep disturbances and mental symptoms. The literature contained most of the facts necessary, when read from the above aspect, to enable us to make drastic changes in our conception and treatment of mental disorders, and to acquire a better understanding of the mind itself.

REFERENCES

[1] Freeman, W. (1933) Neuropathology, p. 256. Philadelphia and London.
[2] Pickworth, F. A. (195)) New Outlook on Mental Diseases Bristol.
[3] Mott, F. W. (1900) The Degeneration of the Neurone, p. 50. Croonian Lecture, London.

Professor McCulloch, in reply, said that he left his research, in problems raised by Organic Neurology while he was at Bellevue Hospital, for less than two years which he had spent in Psychiatry at Rockland State Hospital and from it returned to the laboratory with enough problems to keep him busy for the rest of his life. What he had done in his lecture was to rehearse the classical problems of neuroses, outlining for each neurosis the corresponding experimentation in animals in so far as he knew how to do it. It was his hope that some of his audience would begin to be interested in what one could do with a patient who could not confuse the doctor by his vocabulary.

He took up the questions in the order they were asked. The first concerned the mechanistic approach to the problem of neurosis or of any other psychological activity. One often heard that this or that property of the nervous system could be imitated by machines. Since he had shown that machines can and do have ideas and purposes it did not seem to him to be any great matter to design a machine that objectified itself, which is to have reflective knowledge of its own thinking.

Next, in answer to Dr Richter, who had asked concerning new evidence of resonant circuits, notably the relation of the *Alpha* activity of the brain to the output by mouth,

or by hand and to perceptions. The man, Craik, who held most promise for the world in this direction unfortunately was dead and his work was so buried in Governmental reports that except for his little book it was not accessible. Among his most brilliant work were certain observations of the times during which man took in that amount of information on which he based a predicting response. Craik showed that in some cases it took 2/10ths second, and in others 3/10ths second with a rather sharp break between them, and thereafter the man took in no information during the next 1/10th second. John Stroud, now working with the U.S. Navy, had followed this same line. He showed that man perceived in moments of about 1/10th second each, lacking internal temporal structure and movement, and Stroud was correlating these moments with the electro-encephalographic records. He had shown that these 1/10th second visual moments could be locked in by auditory activity. Anyone who worked with the cathode ray oscilloscope trying to hold a pip in the center of the screen and put the click of the fly-back to his ears by earphones, and turned the frequency to a convenient setting found that he set to his own alpha frequency. The evidence on this was just beginning to come in. There was but one thing he would like to persuade his audience to do namely to collect Craik's work and get it published soon.

With regard to the demons: a demon is not a structure, a demon or a gremlin is but a circuit-action. It is in almost all cases regenerative circuit-action which should be a kind of servomechanism – inverse or negative feedback. It was the peculiar property of complicated circuits like the nervous system that one usually could not precisely locate gremlins in them. Certainly the gremlin is never in a single item without a circuit but always in a closed path. What he had tried to point out was that this gremlin, this resonance, could begin in a disturbed reflex and, if it lived long enough, it modified some other loop and so could give birth to a second demon; whereafter the first demon could die, but, as far as his character or his soul is concerned, receives the same gremlin. He was not sure whether the difficulty the questioner had had was that the lecture attributed mental properties to gremlins who certainly have ideas and intentions.

To Dr Pond's question as to cross-talk and what turns up the gain, the answer was that the cross-talk in a causalgic nerve made it act repetitively and repetitive activity if persistent in some way, turned up the gain of the circuits in the cord. So when we learn to skip or to play a piano, erstwhile inadequate stimuli become adequate though we do not know how repetition turns up the gain. It is difficult to imagine how this happens in the spinal cord where one would expect all connexions to be firmly established by the time one can walk. Yet it seemed now clear that new pathways might be formed or old ones lost under unusual circumstances. This was first reported by Coller and Shurrager, but an excellent neurosurgeon, A. A. Ward, and a psychologist, Donald Marquis, were unable to teach the spinal cord. This suggested to Dr Lettvin that the difference might lie in rough handling, destroying some paths afferent to the motoneuron, thereby leaving it accessible to other impulses. Lettvin, therefore, cut the dorsal roots of a two neuron reflex arc, stimulated afferents normally inhibitory to this arc and simultaneously stimulated antidromically the motoneurons of this two neuron arc. Thereafter the erstwhile inhibitory afferents excited the motoneurons. The reason this work has not been published yet is that we do not know the histologic details nor are we certain the new path is monosynaptic. In any case it shows that the behaviour of the cord can be modified so that formerly inadequate stimuli become adequate. This is one kind of memory. The changes that occur higher in the nervous system may all be due to the kind of memory which preserves snapshots of the world to be re-evoked whenever this is required.

The last question was a crucial one. He did not join in the discussion that morning when Gellhorn lectured although he had wanted to cry 'hear, hear' because Gellhorn was on the right track. He thought neuropsychiatrists had habitually looked to

the cortex for things actually in the brain-stem. Gellhorn was persuading them to look in the right direction. However, the brain-stem was not necessarily the master tissue of the body because there is no one master tissue. Meduna's work had shown that about two-thirds of so-called schizophrenics were biochemically abnormal, being unable to handle glucose properly when given it by vein, and unable to convert levulose into glucose, having something in the blood rendering them resistant to insulin, and putting out in their urine a substance that raised blood sugar in animals. About 1 mg. of this material when purified doubles the blood sugar of a 250-gramme rat. In these disorders of the brain we are dealing with a biochemical disorder which is almost as obscure as diabetes mellitus was when Professor McCulloch was in medical school.

PHYSIOLOGICAL AND PSYCHOLOGICAL RESULTS OF THALAMOTOMY

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Thalamotomy is an attempt to influence disturbances in the emotional sphere by placing circumscribed lesions in the dorsomedial nuclei of the thalamus (dorsomedial thalamotomy) and/or in the hypothalamus (hypothalamotomy). It differs from the various operations in the frontal lobe fundamentally: these latter types of operations interfere not only with the connexions between frontal lobe and thalamus but also with the association systems of the frontal lobe. These association systems are not affected by thalamotomy. The expectation that thalamic lesions may have a favorable effect upon emotional disturbances is based upon Cannon's theory that emotional reactions are due chiefly to an interaction between cortex and diencephalon.

In the selection of the material we were guided by criteria similar to those usually followed for prefrontal lobotomy. 41 patients, mostly institutionalized cases of schizophrenia, depression, severe compulsion neuroses, have been operated upon. Most of these patients were under psychiatric treatment for a period of from one to 17 years, and had also been subjected to the various shock therapies without relief. In 2 patients with obsessive compulsive neurosis, prefrontal lobotomies had been performed at other institutions without alleviating the disturbances. The stereotaxic method used for production of the lesions has been previously described (Spiegel, Wycis, Marks and Lee), and its recent improvements are outlined in a separate paper in this symposium (Wycis and Spiegel).

Types of lesions. – Animal experiments on cats and monkeys convinced us that lesions placed in the dorsomedial nucleus had no harmful effect as far as could be judged from the general appearance and behavior of the animals. There was only in

[1]From the Depts. of Exp. Neurology and Neurosurgery, Temple University School of Medicine and Hospital, Philadelphia, Pa. Including studies by Drs K. B. Conger, H. Keith Fischer, H. Freed, R. Koch, C. Orchinik and H. Shay. The studies of these authors will be published as separate papers.
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some animals a transitory state of somnolence or reduced reactivity. However, since the sequelae of circumscribed lesions of this area in man were not known, we proceeded only step by step, producing in the first group only single coagulations about 3 mm. in diameter and increasing the size and number of the lesions as we became convinced that the operation produced relatively few undesirable by-effects.

Group I: Single lesions (3 cases). In the first case (compulsive obsessive state and depression) we placed only 1 coagulation on each side, in the second patient (catatonic schizophrenia) 4 lesions on the left and 1 on the right, in the 3rd (mental deficiency with agitation) 2 lesions in each dorsomedial nucleus. In view of the smallness of the coagulations, each covering about 1/36 of the volume of the dorsomedial nucleus, one could not expect a definite therapeutic effect from the few lesions placed in this initial group. There was a transitory improvement in Case I, the patient becoming mildly euphoric, less irritable, exhausted and meticulous. This temporary amelioration, however, could hardly be regarded as a consequence of the lesions. These first 3 cases may serve as controls showing that the psychologic or somatic effects of the operative procedures without sufficient lesions of the dorsomedial nucleus are not able to produce permanent changes of emotional tone as seen in patients in whom a larger number of electro-coagulations were produced in each dorsomedial nucleus.

Group II: 5 coagulations in each dorsomedial nucleus through 3 puncture canals (8 cases).

Group III: Large electrolytic lesions consisting of 2–3 rosettes in the dorsal, central and ventral parts of the dorsomedial nucleus produced through 1 single cerebral puncture on each side. Each rosette consists of 4 ovoid lesions, i.e. an anterior, a medial, a posterior and an anterolateral lesion (remaining 30 cases).

Group IV: Hypothalamic lesions. In 7 patients, 1 schizophrenic of group II who had relapsed, and 6 schizophrenics in group III in whom the lesions of the dorsomedial nucleus were insufficient to improve the psychotic state of the patient, 1–3 lesions were placed uni- or bilaterally by means of an electro-coagulation in and above the lateral hypothalamic area through a single puncture canal on each side. In order to minimize shock produced by bilateral hypothalamic lesions the operation was performed in two stages with an interval of several weeks between the first and second operation.

A total of 59 operations was performed in 41 patients. Post-operative death occurred in 1 case in group II and in 1 case in group III, so that the operative mortality was 3·4%.

Initial post-operative symptoms. – While some patients may be awake and oriented on the first day after operation, most exhibit in the first days following dorsomedial thalamotomy similarly as after prefrontal lobotomy, somnolence, disorientation particularly for time, memory defects, inertia, apathy, then psychomotor retardation. These disturbances usually are milder than after the prefrontal lobotomy. It seems particularly of interest that the disorientation affects all spheres after prefrontal lobotomy, while in our material there was chiefly disorientation for time; the patient usually is aware that he is in a hospital and usually does not misidentify persons (except if he was confused before operation). For a few days, he is often not aware that he has been operated upon.

Since the main effect of thalamotomy is found in the emotional sphere, the studies of Rapaport regarding the interrelationship between emotion and memory are of great interest. He considered the possibility that the basic psychological factors underlying the experiencing of emotions are identical with those which come to expression in the form of memory organization attributed to emotional influence. Thus memory organization and emotional experience would be expressions of the same basic factors which may be called psychic energies, strivings, or drives. It seems not

impossible that injury to the thalamofrontal system interferes with these basic psychic factors. However, it should be emphasized that there was no parallelism in the duration of the memory disturbance and the affective relief since the latter usually outlasted the former.

Thus, the possibility cannot be denied that lesions of the dorsomedial nucleus may interfere with diencephalic mechanisms related to a primitive state of consciousness upon which the formation of memory may depend. The lesion of the dorsomedial nucleus may, for instance, affect the functioning of cell groups in the vicinity of the mammillary bodies where pathologic changes have been found in cases of the Korsakoff syndrome (Gudden, Gamper).

Impairment of motility. – There was in 1 case a slight ptosis of one eyelid for two days, in 3 cases an impairment of upward movements of the eyes. This apparently occurred when the lesion reached the posterior parts of the thalamus, close to the mid-brain. In 2 instances a transitory unilateral weakness of the oral branch of the facial nerve developed; there was in 1 patient a slight weakness of one arm for less than one week. The motility of one leg was twice impaired for two to three weeks, once for 2 days; and the Babinski phenomenon was demonstrable in 5 cases of group II for less than two weeks. This was probably due to the fact that the puncture canal passed through the region or the vicinity of the paracentral lobule. In group III, where only one puncture was necessary on each side, there developed only once a weakness of a leg of two days' duration. In 2 cases of group IV a transitory hemiparesis developed. All these motor deficiency symptoms apparently were by-effects caused by encroachment of the lesion to parts outside the dorsomedial nucleus or the hypothalamus. This is indicated by the relatively rare appearance and the short duration of these motor phenomena.

Sensory disturbances. – Disturbances of sensation were still less frequent than impairment of motility. They developed only in group II, once hypalgesia of one arm for five days, once ulnar hyperalgesia for two weeks. This was the only instance in which a symptom resembling the Déjerine thalamic syndrome developed. We tried to prevent the development of such a syndrome by avoiding lesions reaching the ventrolateral parts.

In view of statements in the literature (e.g. Wallenberg) that fibers from the sensory systems may enter the dorsomedial nucleus we tried to ascertain by various methods whether a change in the threshold for painful stimuli developed after dorsomedial thalamotomy. Threshold determinations were performed before and after operation: (1) By applying a metallic brush and measuring the coil distance of an inductorium supplying it with faradic current; (2) by estimating the pressure of stimulating pins; (3) by producing anemia in the arm and ascertaining the number of the flexor-extensor movements of the fingers possible before pain appeared. Significant changes in threshold failed to appear in these 3 series of measurements so that a direct relationship of the dorsomedial muscles to pain perception seems rather doubtful.

There was also no disturbance of the so-called 'psycho-reflexes' (involuntary laughing and crying elicited by emotions) so that a relationship of the dorsomedial nucleus to these reactions assumed by Kirchoff could not be confirmed.

Vegetative system. – The reactivity of the vegetative system was studied by Dr H. Keith Fischer in 15 cases (11 bilateral thalamotomies, 1 pallido-thalamotomy and 3 bilateral mesencephalotomies). The oculo-cardiac reflex, the reaction of blood pressure and pulse to subcutaneous injection of adrenaline, the Loewi adrenaline test, the local reaction to cutaneous adrenaline injection, the atropine test (Daniélopolu modification) and dermographism were tested before and one to two weeks after operation. In the majority of the thalamotomies (7 cases), an increased reactivity of the sympathetic system, particularly to adrenaline injection, e.g. increase of the rise of systolic blood pressure, of pulse rate, and pulse pressure, was observed. In one

instance there was a shift in favor of the parasympathetic system, and 4 patients failed to show post-operative changes. The control cases (3 mesencephalotomies) failed to show definite changes or showed decreased adrenaline reaction. It should be emphasized that the post-operative changes of the resting values definitely influenced the reactivity of pulse or blood pressure to ocular pressure as well as to adrenaline injection, and that the changes in the various reactions (e.g. in blood pressure and pulse rate) did not necessarily always go strictly parallel. Several months after operation the reactivity of the vegetative system again showed the pre-operative pattern. A correlation between the changes in the vegetative reactivity and the therapeutic effects in the emotional sphere could not be established.

The most frequent vegetative by-effect was vesical incontinence (5 cases in group II, 10 in group III); it lasted from a few days to two to three weeks.

In the genesis of this vesical incontinence as well as of the much less frequent rectal incontinence, psychic factors (carelessness, lack of attention) may play a part. But the possibility of changes in the reflex activity of the bladder should not be overlooked. This is indicated by cystometric studies carried out by Dr K. B. Conger. They require, of course, the co-operation of the patient so that it is difficult to apply this method to psychotics, and only in a few cases (7) the measurements appeared reliable.

A definite hypertonicity (hyperirritability) of the bladder developed in 3 cases, and hypertonicity within the range of variability of the method in 1 patient. It should be emphasized that none of these patients showed an involvement of the pyramidal tracts. A decrease of a pre-operative hypertonicity with a tendency to return to normal was observed in 1 case that was complicated by a pre-existing urinary infection, while definite changes failed to appear in 2 patients.

A transient decline of the blood pressure was recorded 4 times after dorsomedial thalamotomy; it was particularly marked in a schizophrenic suffering from vascular hypertension, where a drop from average values of 210/118 to 115/90 occurred. Nine months after operation this patient still showed lowered blood-pressure values varying between 136/82 and 155/90.

In 3 patients of groups II and III, there was a definite increase of appetite and weight.

The blood lipids (cholesterol, phospholipids, fatty acids, neutral fats), the various liver function tests and the glucose tolerance before and after dorsomedial thalamotomy were studied by Dr H. Shay (14 cases). Following this procedure, changes were found only in regard to the latter test. In 4 cases with peak blood sugar values above 180 mg. within one hour after ingestion of glucose, there was within two weeks to two months following thalamotomy a decrease of the postprandial hyperglycemia. This effect was only transitory. Six months after operation, the glucose tolerance curve returned to the pre-operative values. In cases with less marked postprandial hyperglycemia (8 thalamotomies, 2 mesencephalotomies), the glucose tolerance failed to show significant changes after the operative procedure.

The relatively short duration of most of the vegetative changes suggests that the lesions placed in the dorsomedial nucleus temporarily affect the activity of hypothalamic centers. Further studies will have to analyse whether this is caused by a reduction or loss of stimulating impulses from the dorsomedial nucleus to cortical or hypothalamic vegetative centers or the effect of shock upon these areas. A certain indication that such an effect of shock upon the hypothalamic centers produced by the lesion in the dorsomedial nucleus is not the only factor, is given by the fact that the small electrocoagulations that we placed in the lateral hypothalamic area (*see later*) produced only rather slight vegetative disturbances.

Emotional changes. – Beneficial effects upon pathologic symptoms were obtained chiefly in the emotional sphere. In successfully operated cases, the patients' anxiety,

tension, and worry disappeared or were at least definitely reduced. They became more easily manageable, their agitation, aggressive or assaultive behavior subsided. Hallucinations were reduced, lost their emotional charge, occasionally even disappeared. The same applies to paranoid ideas. Obsessive thinking also lost its force and compulsive activity disappeared.

The development of this improvement sometimes became manifest after an interval of several weeks. In the intermediary stage, repressed symptoms such as hostility or increased libido may become manifest for a while; this was particularly obvious in two catatonic schizophrenics (Nos. 19 and 27).

The question may be raised why not only tension and anxiety are relieved, but also such symptoms as delusions and hallucinations. If one recognizes with Bleuler the dominant role of affectivity among psychic functions and the influence of emotional disturbances in the genesis of pathological associations, it may become plausible that lessening of tension and anxiety may also favorably influence pathological associations and related symptoms. However, it should be emphasized that operative procedures relieving emotional disturbances and allied phenomena do not eliminate the as yet unknown basic disturbances underlying dementia praecox.

The reduction of anxiety may manifest itself also by a drop in the score of Garrison's anxiety and complaint inventory as well as in Rorschach studies.

The Rorschach data of 9 cases were analysed by Mr C. W. Orchinik who arrived at the following conclusions: these patients show a rather limited pre-operative productivity (R); immediately after operation, the average number of responses increased; however, this liberation from constriction is transitory. Individual cases of extreme constriction are less constricted after operation. The changes in the number of responses occurring after the operation seem to vary with the pre-operative personality structure. There is some pre-operative constriction in inner life (average pre-operative responses with human movement (M) slightly less than 2). This tends to persist post-operatively for the group. In cases who did not have an M pre-operatively, there is a tendency for an M to appear. This suggests a trend toward increased reflectiveness in patients in whom it was previously absent. There is a rather meager outer life pre- and post-operatively as indicated by the relatively small number of responses in which color is a determinant. However, slight changes are noted post-operatively such as increase of reactions with fusion of form and color (FC), indicating a tendency toward greater emotional adaptability. Regarding post-operative changes of CF responses (in which color is the major determinant and form secondary) and of C responses (in which color alone is the determinant) valid conclusions cannot be drawn, because too few cases showed any CF or C pre- or post-operatively. Control is moderately high (F responses primarily determined by form, fairly high) and remains about the same post-operatively. There is some improvement in the quality of the form responses post-operatively. This indicates better integration of the personality. Instinctual drives are present as shown by responses of animals in movement (FM). Immature trends seem to outweigh the mature ones both before and after operation, as indicated by the prevalence of FM over M responses. There was a tendency to overgeneralize in the pre-operative record (responses to the whole blot W almost 50%), which seems to decrease post-operatively. Practical, more conventional thinking seems to go up after operations (about 60% responses to details D in post-operative test II). Some dilatation in personality particularly in emotional adaptivity and responsivity is suggested by the tendency to increase in FC reactions after operation. But the basic structure of the group as indicated by the graph as a whole remains essentially the same. No consistent gross changes in the personality appear for this group.

The findings seem to indicate that in some cases patients who have difficulty coping with emotionally charged situations pre-operatively are better able to meet these

situations after thalamotomy; the emotional situation is no longer so upsetting as it was pre-operatively and the patient does not feel the weight of the problems so intensely.

Examination of 5 cases which showed improvement after thalamotomy seems of particular interest. It reveals some similarity in the pre-operative records, particularly some manifestations of color and shading shock, psychoneurotic symptoms revealed in the Rorschach by delayed reaction time to the cards, rejection of the cards, or exclamations. After operation these symptoms decrease or are less intense. For example, in 3 cases there was a marked delay in reaction time to the cards pre-operatively. Several months after operation this shock reaction time decreased noticeably, especially the reaction time to the color cards. That these changes are not the result of practice is suggested by the length of time which elapsed between re-testing. These cases will be discussed in another paper in which individual as well as group changes will be evaluated.

It may be asked whether the relief of affective disorders following the thalamic lesions is only the consequence of destruction of brain substance, or whether it depends on lesion of a definite area such as the region of the dorsomedial nucleus. In this respect a case seems of interest in whom the first lesion was inadvertently produced in the posterior part of the thalamus in the vicinity of the corpora quadrigemina due to a displacement of the base of the stereo-encephalotome. The location of the lesion was indicated by a droplet of pantopaque injected at the end of the operation as well as by impairment of the upward movement of the eyeballs and loss of the light reflex of the pupils. This lesion failed to influence the psychotic picture of the patient, her suspicious and paranoid attitude. Following a second operation performed several weeks later in the region of the dorsomedial nucleus the patient became co-operative and friendly and seemed no longer suspicious or paranoid.

Social adaptability. – 33 patients in groups II and III (extensive lesions of the dorsomedial nuclei) were observed for over three months (from four months to over two years). Of these 33 patients, 5 returned home with nearly full working capacity, 11 returned home with diminished working capacity, 9 were more manageable in the hospital, 8 are unchanged, and of the 16 with definite improvement 6 have relapsed[1].

The appearance of relapses may have various causes, partly psychologic, such as increase of the stress to which the patient is subjected after leaving the protective atmosphere of the hospital and returning to daily life, and partly anatomic-physiologic causes. Our main goal in the first part of our work was to ascertain the minimum lesion able to produce a therapeutic effect. We were therefore satisfied in group II to place 5 small lesions covering about one-seventh of the volume of the dorsomedial nuclei. However, after placing larger lesions (3 layers of rosettes in each dorsomedial nucleus) we also observed some relapses. In analysing their development the following has to be borne in mind: It is rather improbable that the neural mechanism of such a complex function like emotions is limited to a single system such as the connexions between the dorsomedial nucleus of the thalamus and the frontal association areas, and it seems rather probable that also other systems may participate in this mechanism. One may consider the possibility that particularly hypothalamic connexions with the frontal lobes, perhaps by way of the septum or those with areas on the orbital surface shown by strychnine neuronography (Ward and McCulloch) may play a part in this mechanism, besides the connexion of the dorsomedial nucleus with the frontal association areas. One has, therefore, to bear in mind the possibility that even following large lesions of the dorsomedial nuclei compensatory mechanisms may take place, and

[1]In this respect the experiences with the much more extensive prefrontal leucotomy are of interest. In the material reviewed by the Board of Control (England and Wales), 11·5% of the schizophrenics who recovered or improved following the operation relapsed. In Freeman and Watts' material, observed for a ten-year period, the relief following the first operation was only transitory in 12 of 20 cases.

that the development of such compensation may be one of the causes of the relapses.

Comparison of stimulation of the hypothalamus and of the dorsomedial nucleus. – The assumption that the hypothalamus may compensate for the loss of the dorsomedial nuclei and that its role in the mechanism of emotions may be more important than that of the dorsomedial nuclei is supported by a comparison of the effects of stimulation of these 2 areas. In 2 patients, one epileptic and a psychoneurotic with anxiety state, we had an opportunity to stimulate the dorsomedial nucleus in local anaesthesia with an interrupted D.C. (14 interruptions/second). The first patient stated during stimulation, that he had a feeling of weakness but no other abnormal sensations or feelings. The second patient stated during stimulation that he felt 'different, dizzy', but he also failed to experience a definite sensation or excitement. This is in contrast to Foerster's observations that stimulation of the floor of the third ventricle may produce manic reactions and Grinker's experiences that stimulation of the base of the brain from the roof of the pharynx may produce anxiety. However, it should not be overlooked that, in some instances (White), stimulation of the hypothalamus may also fail to produce psychic changes. Furthermore, stimulation of frontal areas connected to the dorsomedial nuclei, also does not produce emotional reactions, although their extirpation may be followed by relief from anxiety (Mettler).

Hypo- and sub-thalamic lesions. – Particularly animal experiments induced us to place lesions in the sub- and hypo-thalamus in cases who relapsed following initial improvement after dorsomedial thalamotomy or in whom such a procedure proved insufficient. In experiments of Spiegel and Miller, subthalamic lesions in cats produced a transient somnolence and catalepsy and the animals were less excitable than before operation. In monkeys, Ranson observed, following bilateral lesions of the lateral hypothalamic areas, that the emotional reactions decreased.

In 7 schizophrenics, we placed 1–3 electrocoagulations through 1 puncture canal in the lateral hypothalamic area and the overlying subthalamus. The first case of this type may be briefly described.

This was an agitated, hallucinating schizophrenic who had improved to such an extent after the first thalamotomy that he could be considered nearly normal. One and a half years after the operation he relapsed, again hallucinated, and had to be readmitted in view of his catatonic excitement. Since a second thalamotomy increasing the lesion of the dorsomedial nuclei failed to change his condition, it was decided to place a small lesion on either side in the lateral hypothalamus in a two-stage operation. Following this procedure, he quieted down, did no longer hallucinate, and became easily manageable. Although he still showed schizophrenic traits, laughed inappropriately, he could be discharged from the hospital, and his parents now try to readjust him on a farm.

In a second agitated hallucinating schizophrenic, it was also necessary to add bilateral hypothalamic lesions to those of the dorsomedial nuclei. In 5 other cases, the addition of unilateral (right-sided) hypothalamotomy to the bilateral dorsomedial thalamotomy seemed sufficient. In one of these cases, bilateral dorsomedial thalamotomy was combined with right-sided hypothalamotomy in a one-stage operation. In all these cases, these combined operations were able to relieve the patients from anxiety, emotional overexcitability, agitation, so that they became quiet and more easily manageable. A second patient could be sent home. For the others the time of observation is too short to arrive at a definite conclusion.

The effects of these hypothalamic punctures upon the vegetative system were surprisingly slight. There was in all cases a transitory rise in temperature lasting from one to two days up to over a week. In some instances there was a slight anisocoria which could be detected in diffuse light only, and a transitory slight vasodilatation in the opposite limbs revealed by a slight increase of skin temperature on the opposite side. Contrary to Ranson's monkeys who refused food and were nauseated after

bilateral hypothalmic lesions, most of our patients showed an excellent appetite a few days after the operation. Only 1 was nauseated. Transitory polydipsia and polyuria appeared in 2 cases. Somnolence was marked for a few days to over a week in all cases, and in 1 patient there was a transitory state of catalepsy.

Undesirable side-effects of long duration. – Since our longest observation period after hypothalamotomy is five months, a discussion of long-lasting undesirable side-effects is limited to those cases in which dorsomedial thalamotomy was performed only. In 4 cases there were defects of memory lasting for several months and in 3, a diminution of initiative. One of these patients had been previously subjected to prefrontal lobotomy at another hospital. This latter patient is also more careless in personal appearance.

Psychometric tests[1]. – The data obtained by administering the Wechsler-Bellevue Intelligence Scale on 16 individuals before and after dorsomedial thalamotomy, in 3 before and after mesencephalotomy, and in 3 before and after paracommissural thalamotomy within one to three weeks and three months after operation were analysed by Miss R. Koch.

The statistical analysis of our material as well as a comparison with Hamister's data of S.D.'s S.Em.'s for the subtests and the various scales in a neuropsychiatric population showed that the differences in the mean achievement before and after operation in subtest scores, verbal I.Q., performance I.Q., and full scale I.Q. are statistically insignificant and ought to be attributed to chance factors or sampling variations. Regarding the results in individual cases, the full scale I.Q. dropped in 3 patients in the first post-operative test but recovered in the second and/or third test; one schizophrenic showed a decline that was more pronounced in the second than in the first post-operative test, apparently due to a progress of the basic disease. A marked increase of the total I.Q., e.g. in an obsessive compulsive-neurotic from 85 to 105 in the second post-operative test, may be due to the fact that such a patient becomes better able to concentrate on the task if he is no longer dominated by fears or obsessive thinking.

One of the main objections raised against psychosurgery is the pronounced personality change, which has been described by the statement that the patient 'loses his soul'. It would seem that one of the chief advantages of thalamotomy is that a relief of emotional disorders may be obtained, and that most of the long-lasting undesirable personality changes following prefrontal lobotomy such as distractibility, childishness, facetiousness, or a lack of tact or discipline, profanity, outbursts of temper do not appear.

Post-operative convulsions. – The method seems to have the further advantage that only a minimum scarring of the cortex is produced by introducing a thin electrode. This is in contrast to the extensive scars in the cortex and white matter produced by the various types of operations in the frontal lobe which lead to epileptiform convulsions in a rather high percentage of the patients. In our material, Jacksonian convulsions appeared only once, in Case 4, in whom bilateral dorsomedial thalamotomy and hypothalamotomy had been performed. Several months after the last operation, a suppurative infection of the upper lid of the left eye developed. During this latter illness a right-sided seizure of clonic convulsions appeared. A definite relationship of this suppuration to the operation could not be established.

EEG studies. – The EEG taken at various intervals, from fifteen minutes up to nearly two years, after operation failed to show signs of an increased convulsive reactivity. In many instances, there were no significant post-operative changes of the rhythm. In some cases there developed after extensive lesions of the dorsomedial nuclei or after combination of such lesions with hypothalamotomy slowing, particularly in the

[1]Part of the psychometric and Rorschach studies was carried out by Mrs F. Nasife, Mrs C. Krusen-Scholtz, Miss J. V. Trasoff, and Miss P. C. Walsh.

frontal leads, which subsided within a few weeks. This confirms experiments on cats (Spiegel, Bremer) showing that *a* activity may still appear in the electrocorticogram, if the circuits between the frontal lobe and the thalamus are interrupted.

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DISCUSSION

Dr DENIS HILL said that with regard to the experiment of cutting connexions between the dorsomedial nucleus and the cortex in relation to it, the thalamus was not disconnected from the cortex, only part of the connexions were severed, and it was difficult to assume that because such part was severed that necessarily all the connexions with the thalamus were severed and that for this reason the spontaneous activity of the cortex should disappear. Spontaneous activity of the cortex was also dependent upon the hypothalamus. The question he asked himself was whether this work fitted in with the work of Professor Gellhorn. The latter with Dr J. P. Murphy had shown that the pathway for excitation of the cortex from the hypothalamus went through the dorsomedial nucleus where it was relayed, and perhaps what Professor Spiegel had done was to interrupt this excitatory pathway. A point in its favour was that there was greater excitability of certain functions after operation. The inhibitory action of the cortex upon the hypothalamus was reduced.

He would be interested to hear Professor Spiegel's comments on the work of Professor Gellhorn in relation to his own work.

Dr TURNER MCLARDY asked whether he had understood Professor Spiegel correctly to say there was evidence that there were no collateral connexions from the sensory systems to the dorsomedial nucleus of the thalamus? If so, did he intend that statement to apply also to the possibility of relay of impulses by way of intrathalamic internuncial neurones from, for instance, ventralis posterior to the dorsomedian? He himself had seen very suggestive histological evidence of the existence of such neurones.

He was interested to hear of the appearance of delta rhythm activity in the frontal regions for a period of one week to one month following such focal thalamic damage. This finding would support the anatomical work being done by silver-impregnation technique on corticofugal connexions between prefrontal cortex and thalamus, for it was just the period during which one would expect retrograde degeneration of cells in the cortex after cutting of their axons within the thalamus. It therefore supported the evidence for the existence of two-way point-to-point connexion between thalamic nuclei and cortex, connexions on which the validity of 'reverberating circuit' concepts largely depended.

Professor SPIEGEL, in reply, said that he did not know to what extent they had destroyed the dorsomedial nuclei, but in a number of instances rather extensive lesions were produced; in the animal experiments there was certainly a complete disconnexion of the frontal lobes from the thalamus, and he still observed alpha activity in these preparations, a little slower and more irregular than normally but it seemed that the connexions between the frontal lobe and the thalamus were not necessary for the maintenance of rhythmic cortical activity. It may be of interest to compare the finding of the thalamic seizure discharges in cases of *petit mal* with Jasper's animal experiments. Jasper found that cortical spike and dome discharges could be produced by stimulation of the region of the internal lamina medullaris. Professor Spiegel did not show all the records in order to save time, but the maximum activity was not necessarily in the region of the lamina medullaris interna but in the more dorsal areas of the thalamus. In other words, the focus of thalamic seizure discharges is not necessarily confined to the internal lamina medullaris, but may cover a larger area. This was supported by some work on *petit mal* cases in which Dr Wycis and he tried to suppress the *petit mal* attacks by placing lesions in the region of the commissura media. That reduced or suppressed to a certain extent the *petit mal* attacks, in one case for a long time, in other cases the *petit mal* attacks returned, which made him believe that rather extensive lesions had to be produced in order to suppress the *petit mal* attacks. It was quite possible that the lesion of the dorsomedial nucleus interrupts the system described by Gellhorn, and the transitory slowing of the EEG which had been shown might be in agreement with such an assumption. The fact that this transitory slowing was found not only in the frontal lobes but in the other parts of the cortex suggests that the lesion affected the system on stimulation of which Morison and Dempsey induced recruiting potentials widespread in the cerebral cortex; but he would emphasize that the slowing was only transitory.

With regard to the question of collaterals from the sensory systems, this could not be decided on his material. He could only say that it did not show significant changes in threshold and one would expect to a certain extent to find some threshold changes if collaterals from sensory systems were affected. This question needed electrographic and histological investigation. With regard to cytoarchitectonic changes in the cortex some studies were made by Dr Kuhlenbeck on monkeys in whom the dorsomedial nuclei had been injured in order to see if there were retrograde changes in the cortex, and he was surprised to find that they were rather slight. It seemed that the relationship between the thalamofrontal and frontothalamic fibers was that the former are more important than the latter, at least in monkeys.

VOTE OF THANKS

Sir HENRY DALE (President of the Royal Society of Medicine) expressed the gratitude of all present to the American colleagues who had taken the opportunity of their visit to Europe to give the members of the Society such a rare feast of knowledge and ideas. He had not expected, in fact, to take any part in the meeting, except to take the Chair that morning; but he had found the whole atmosphere of the discussion so intensely stimulating, and it had been for him such a wonderful experience, that he had found himself, to his own surprise, sitting through the whole series of meetings. He was sure that there were many who had had the same feelings; and he hoped that he would be allowed to express their thanks to all those who had taken part, who had read the papers, and had contributed to the discussions, which he was sure would have a lasting effect on experimental work in this field of psychiatry in this country.

The vote of thanks was accorded by applause, and a further vote of thanks was accorded to Dr William Sargant for his work in arranging the meeting.

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